Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	14	(amyloid near4 peptide) same (diameter or aggregrate)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L2	4	l1 same length	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L3	91	(amyloid near4 peptide) and (diameter same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:49
L4	36	l3 and glutamine	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 13:50

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g repeat) and aggregrate and length and diameter
0 FILE AGRICOLA
0 FILE BIOTECHNO
0 FILE CONFSCI
0 FILE HEALSAFE
0 FILE IMSDRUGCONF
0 FILE LIFESCI
0 FILE MEDICONF
0 FILE PASCAL

FOR ALL FILES
0 (CAG REPEAT) AND AGGREGRATE AND LENGTH AND DIAMETER

e .chemistry
N U.S. DOLLARS

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=> (cag repeat) and aggregrate and length and diameter
L10 0 FILE CAPLUS
L11 0 FILE BIOTECHNO
L12 0 FILE COMPENDEX
L13 0 FILE ANABSTR
L14 0 FILE CERAB
L15 0 FILE METADEX
L16 0 FILE USPATFULL

TOTAL FOR ALL FILES
L17 0 (CAG REPEAT) AND AGGREGRATE AND LENGTH AND DIAMETER

=> glutamine and aggregrate and length and diameter
L18 0 FILE CAPLUS
L19 0 FILE BIOTECHNO
L20 0 FILE COMPENDEX
L21 0 FILE ANABSTR
L22 0 FILE CERAB
L23 0 FILE METADEX
L24 1 FILE USPATFULL

TOTAL FOR ALL FILES
L25 1 GLUTAMINE AND AGGREGRATE AND LENGTH AND DIAMETER

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregrate or assembly) and length
L26 2 FILE CAPLUS
L27 1 FILE BIOTECHNO
L28 0 FILE COMPENDEX
L29 0 FILE ANABSTR
L30 0 FILE CERAB
L31 0 FILE METADEX
L32 50 FILE USPATFULL

TOTAL FOR ALL FILES
L33 53 (CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH

=> dup rem
ENTER L# LIST OR (END):l26-l27
PROCESSING COMPLETED FOR L26
PROCESSING COMPLETED FOR L27
L34 3 DUP REM L26-L27 (0 DUPLICATES REMOVED)

=> d l34 ibib abs total

L34 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:716876 CAPLUS
DOCUMENT NUMBER: 139:287912
TITLE: **Ataxin**-3 interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis
AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran
CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA
SOURCE: Molecular and Cellular Biology (2003), 23(18),

6469-6483
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin**-3. We investigated whether **ataxin**-3 is a proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin**-3 interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin**-3 assocs. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin**-3 is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelier, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzel, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington**'s disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β-sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	605	pauline.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:14
L2	1158	paulson.in.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:15
L3	2	l2 and ataxin	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2004/12/16 10:17
L4	0	ataxin same glutamine same filament	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:17
L5	55	glutamine same filament	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:17
L6	1	glutamine same filament same diameter	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:18
L7	9	(glutamine same repeat) and (filament same diameter)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:44
L8	25	(glutamine same repeat) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:54
L9	4885	(poly(gln) or polyglutamine) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:55
L10	15	("poly(gln)" or polyglutamine) and (filament same length)	US-PGPUB; USPAT; EPO; DERWENT	OR	ON	2004/12/16 10:56

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                          ENTRY     SESSION
FULL ESTIMATED COST                                        0.21        0.21

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=> (polyglutamine or poly(glu)) and filament and length and diameter
MISSING OPERATOR 'POLY(GLU'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> (polyglutamine or "poly(glu)") and filament and length and diameter
L1             0 FILE AGRICOLA
L2             0 FILE BIOTECHNO
L3             0 FILE CONFSCI
L4             0 FILE HEALSAFE
L5             0 FILE IMSDRUGCONF
L6             0 FILE LIFESCI
L7             0 FILE MEDICONF
L8             0 FILE PASCAL

TOTAL FOR ALL FILES
L9             0 (POLYGLUTAMINE OR "POLY(GLU)") AND FILAMENT AND LENGTH AND DIAME
                 TER

=> polyglutamine and filament and length and diameter
L10            0 FILE AGRICOLA
L11            0 FILE BIOTECHNO
L12            0 FILE CONFSCI
L13            0 FILE HEALSAFE
L14            0 FILE IMSDRUGCONF
L15            0 FILE LIFESCI
L16            0 FILE MEDICONF
L17            0 FILE PASCAL

TOTAL FOR ALL FILES
L18            0 POLYGLUTAMINE AND FILAMENT AND LENGTH AND DIAMETER
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=> polyglutamine and filament and length
L19           0 FILE AGRICOLA
L20           3 FILE BIOTECHNO
L21           0 FILE CONFSCI
L22           0 FILE HEALSAFE
L23           0 FILE IMSDRUGCONF
L24           1 FILE LIFESCI
L25           0 FILE MEDICONF
L26           1 FILE PASCAL

TOTAL FOR ALL FILES
L27           5 POLYGLUTAMINE AND FILAMENT AND LENGTH

=> dup rem
ENTER L# LIST OR (END):l27
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L27
L28            4 DUP REM L27 (1 DUPLICATE REMOVED)

=> d l28 ibib abs total

L28  ANSWER 1 OF 4  LIFESCI    COPYRIGHT 2004 CSA on STN
ACCESSION NUMBER:   2003:45445  LIFESCI
TITLE:              Amyloid-like Features of Polyglutamine Aggregates
                    and Their Assembly Kinetics
AUTHOR:             Chen, Songming; Berthelier, V.; Hamilton, J.B.; O'Nuallain,
                    B.; Wetzel, R.
CORPORATE SOURCE:   Graduate School of Medicine, University of Tennessee
                    Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920,
                    USA
SOURCE:             Biochemistry (Washington) [Biochemistry (Wash.)], (20020611
     )              vol. 41, no. 23, pp. 7391-7399.
                    ISSN: 0006-2960.
DOCUMENT TYPE:      Journal
FILE SEGMENT:       N3
LANGUAGE:           English
SUMMARY LANGUAGE:   English
AB   The repeat length-dependent tendency of the
     polyglutamine sequences of certain proteins to form aggregates may
     underlie the cytotoxicity of these sequences in expanded CAG repeat
     diseases such as Huntington's disease. We report here a number of features
     of various polyglutamine (polyGln) aggregates and their assembly
     pathways that bear a resemblance to generally recognized defining features
     of amyloid fibrils. PolyGln aggregation kinetics displays concentration
     and length dependence and a lag phase that can be abbreviated by
     seeding. PolyGln aggregates exhibit classical beta -sheet-rich circular
     dichroism spectra consistent with an amyloid-like substructure. The
     fundamental structural unit of all the in vitro aggregates described here
     is a filament about 3 nm in width, resembling the protofibrillar
     intermediates in amyloid fibril assembly. We observed these filamentous
     structures either as isolated threads, as components of ribbonlike sheets,
     or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates
     described here bind thioflavin T and shift its fluorescence spectrum.
     Although all polyGln aggregates tested bind the dye Congo red, only
     aggregates of a relatively long polyGln peptide exhibit Congo red
     birefringence, and this birefringence is only observed in a small portion
     of these aggregates. Remarkably, a monoclonal antibody with high
     selectivity for a generic amyloid fibril conformational epitope is capable
     of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of
     the characteristic features of amyloid, but the twisted fibril structure
     with Congo red birefringence is not the predominant form in the polyGln
     repeat length range studied here. We also find that polyGln
     peptides exhibit an unusual freezing-dependent aggregation that appears to
```

be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the molecular structure of the product. This ordered structure, or the assembly process leading to it, may be responsible for the cell-specific neuronal degeneration observed in Huntington's and other expanded CAG repeat diseases.

L28 ANSWER 2 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded **polyglutamine** domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO

AB Eight inherited neurodegenerative diseases are caused by genes with expanded CAG repeats coding for **polyglutamine** domains in the disease- producing proteins. The mechanism by which this expanded **polyglutamine** domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic **polyglutamine** protein aggregation is a common feature. In transfected COS7 cells, expanded **polyglutamine** proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length polyglutamine** domain proteins also interact with NF. We expressed varying **lengths polyglutamine**-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length polyglutamine**-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-**length polyglutamine** proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that **polyglutamine** interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L28 ANSWER 3 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1999:30038076 BIOTECHNO
TITLE: **Polyglutamine** domain proteins with expanded repeats bind neurofilament, altering the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Annals of the New York Academy of Sciences, (1999), 893/- (192-202), 49 reference(s)
CODEN: ANYAA0 ISSN: 0077-8923
DOCUMENT TYPE: Journal; Conference Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AN 1999:30038076 BIOTECHNO
AB Proteins with expanded **polyglutamine** (polyQ) repeats cause eight inherited neurodegenerative diseases. Nuclear and cytoplasmic polyQ protein is a common feature of these diseases, but its role in cell death remains debatable. Since the neuronal intermediate **filament** network is composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic **length** polyQ domain proteins interact with NF. We expressed polyQ-green fluorescent fusion proteins (GFP) in a neuroblast cell line, TR1. Pathologic-**length** polyQ-GFP fusion proteins form large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic **length** polyQ proteins co-isolated 68 kD NF protein demonstrating molecular interaction. These observations suggest that polyQ interaction with NF is important in the pathogenesis of the **polyglutamine** repeat diseases.

L28 ANSWER 4 OF 4 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1997:27464435 BIOTECHNO
TITLE: Oligomerization of expanded-**polyglutamine** domain fluorescent fusion proteins in cultured mammalian cells
AUTHOR: Onodera O.; Burke J.R.; Miller S.E.; Hester S.; Tsuji S.; Roses A.D.; Strittmatter W.J.
CORPORATE SOURCE: W.J. Strittmatter, Department of Medicine (Neurology), Duke University Medical Center, Durham, NC 27710, United States.
E-mail: warren@neuro.duke.edu
SOURCE: Biochemical and Biophysical Research Communications, (1997), 238/2 (599-605), 29 reference(s)
CODEN: BBRCA0 ISSN: 0006-291X
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1997:27464435 BIOTECHNO
AB Six inherited neurologic diseases, including Huntington's disease, result from the expansion of a CAG domain of the disease genes to produce a domain of more than 40 glutamines in the expressed protein. The mechanism by which expansion of this **polyglutamine** domain causes disease is unknown. Recent studies demonstrated oligomerization of **polyglutamine**-domain proteins in mammalian neurons. To study oligomerization of **polyglutamine** proteins and to identify heterologous protein interactions, varying **length** **polyglutamine**-green fluorescent protein fusion proteins were expressed in cultured COS-7 cells. The 19-and 35-glutamine fusion proteins (non-pathologic **length**) distributed diffusely throughout the cytoplasm. In contrast, 56- and 80-glutamine fusion proteins (pathologic **length**) formed fibrillar arrays resembling those previously observed in neurons in Huntington's disease and in a transgenic mouse model. These aggregates were intranuclear and intracytoplasmic. Intracytoplasmic aggregates were surrounded by collapsed intermediate **filaments**. The intermediate **filament** protein vimentin co-immunoisolated with expanded **polyglutamine** fusion proteins. This cellular model will expedite investigations into oligomerization of **polyglutamine** proteins and their interactions with other proteins.

=> wetzel r/au
L29 13 FILE AGRICOLA
L30 38 FILE BIOTECHNO
L31 19 FILE CONFSCI
L32 1 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE

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L33           0 FILE IMSDRUGCONF
L34          32 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L35           0 FILE MEDICONF
L36          91 FILE PASCAL

TOTAL FOR ALL FILES
L37         194 WETZEL R/AU

=> yang w/au
L38          61 FILE AGRICOLA
L39         273 FILE BIOTECHNO
L40         107 FILE CONFSCI
L41           5 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE
L42           0 FILE IMSDRUGCONF
L43         175 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L44           0 FILE MEDICONF
L45         356 FILE PASCAL

TOTAL FOR ALL FILES
L46         977 YANG W/AU

=> l37 and l46
L47           0 FILE AGRICOLA
L48           2 FILE BIOTECHNO
L49           0 FILE CONFSCI
L50           0 FILE HEALSAFE
L51           0 FILE IMSDRUGCONF
L52           0 FILE LIFESCI
L53           0 FILE MEDICONF
L54           0 FILE PASCAL

TOTAL FOR ALL FILES
L55           2 L37 AND L46

=> d l55 ibib abs total'
'TOTAL'' IS NOT A VALID FORMAT FOR FILE 'BIOTECHNO'

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BIB   ------- AN, TI, AU, CS, SO, PUI, DT, CY, LA, SL
IBIB ---------- BIB, indented with text labels
ALL   ------- AN, TI, AU, CS, SO, PUI, DT, CY, LA, SL, AB, CT, RN, CN, TN, CO, GEN
IALL ---------- ALL, indented with text labels
DALL ---------- ALL, delimited (end of each field identified)
ABS   ------- AN, AB
IND   ------- AN, CT, RN, CN, TN, CO, GEN
TRIAL ------- AN, TI, CT
SAM   ------- AN, TI, CT
SAMPLE   ------- AN, TI, CT
TRI   ------- AN, TI, CT
To display a particular field or fields, enter the display field codes. For a list
of display field codes, enter 'HELP DFIELDS' at an arrow prompt (=>). Examples of
formats include: 'TI'; 'AN,TI,AU'; 'BIB,CT'; 'TI,CT'.
The order of the terms in the formats is not important, but information will be
displayed in the same order as the format specification.
The same formats may be used with the DISPLAY AN  command to display the record for
a specified accession number.
FREE   ------- AN, TI, CT
ENTER DISPLAY FORMAT (BIB):bib

L55   ANSWER 1 OF 2  BIOTECHNO  COPYRIGHT 2004 Elsevier Science B.V. on STN
```

AN 2002:35331822 BIOTECHNO
TI Aggregated polyglutamine peptides delivered to nuclei are toxic to mammalian cells
AU **Yang W.**; Dunlap J.R.; Andrews R.B.; **Wetzel R.**
CS R. Wetzel, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States. E-mail: rwetzel@mc.utmck.edu
SO Human Molecular Genetics, (01 NOV 2002), 11/23 (2905-2917), 51 reference(s)
CODEN: HMGEE5 ISSN: 0964-6906
DT Journal; Article
CY United Kingdom
LA English
SL English

=> d l55 ibib abs total

L55 ANSWER 1 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2002:35331822 BIOTECHNO
TITLE: Aggregated polyglutamine peptides delivered to nuclei are toxic to mammalian cells
AUTHOR: **Yang W.**; Dunlap J.R.; Andrews R.B.; **Wetzel R.**
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States. E-mail: rwetzel@mc.utmck.edu
SOURCE: Human Molecular Genetics, (01 NOV 2002), 11/23 (2905-2917), 51 reference(s)
CODEN: HMGEE5 ISSN: 0964-6906
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:35331822 BIOTECHNO
AB A number of observations point to the aggregation of expanded polyglutamine [poly(Q)]-containing proteins as playing a central role in the etiology of Huntington's disease (HD) and other expanded CAG-repeat diseases. Transfected cell and transgenic animal models provide some of this support, but irrefutable data on the cytotoxicity of poly(Q) aggregates is lacking. This may be due in part to difficulties in observing all aggregated states in these models, and in part to the inability to conclusively rule out the role of monomeric states of the poly(Q) protein. To address these questions, we produced aggregates of simple poly(Q) peptides in vitro and introduced them to mammalian cells in culture. We find that Cos-7 and PC-12 cells in culture readily take up aggregates of chemically synthesized poly(Q) peptides. Simple poly(Q) aggregates are localized to the cytoplasm and have little impact on cell viability. Aggregates of poly(Q) peptides containing a nuclear localization signal, however, are localized to nuclei and lead to dramatic cell death. Amyloid fibrils of a non-poly(Q) peptide are non-toxic, whether localized to the cytoplasm or nucleus. Nuclear localization of an aggregate of a short, Q.sub.2.sub.0, poly(Q) peptide is just as toxic as that of a long poly(Q) peptide, supporting the notion that the influence of poly(Q) repeat length on disease risk and age of onset is at the level of aggregation efficiency. The results support a direct role for poly(Q) aggregates in HD-related neurotoxicity.

L55 ANSWER 2 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32735322 BIOTECHNO
TITLE: Polyglutamine aggregation behavior in vitro supports a recruitment mechanism of cytotoxicity
AUTHOR: Chen S.; Berthelier V.; **Yang W.**; **Wetzel**

R.
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Journal of Molecular Biology, (03 AUG 2001), 311/1 (173-182), 54 reference(s)
CODEN: JMOBAK ISSN: 0022-2836
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32735322 BIOTECHNO
AB In expanded CAG repeat diseases such as Huntington's disease, proteins containing polyglutamine (poly(Gln)) sequences with repeat lengths of about 37 residues or more are associated with development of both disease symptoms and neuronal intranuclear inclusions (NIIs). Disease physiology in animal and cellular models does not always correlate with NII formation, however, and the mechanism by which aggregate formation might lead to cytotoxicity is unknown. To help evaluate various possible mechanisms, we determined the biophysical properties of a series of simple poly(Gln) peptides. The circular dichroism spectra of poly(Gln) peptides with repeat lengths of tive, 15, 28 and 44 residues are all nearly identical and are consistent with a high degree of random coil structure, suggesting that the length-dependence of disease is not related to a conformational change in the monomeric states of expanded poly(Gln) sequences. In contrast, there is a dramatic increase in both the kinetics and the thermodynamic favorability of the spontaneous formation of ordered, amyloid-like aggregates for poly(Gln) peptides with repeat lengths of greater than 37 residues. At the same time, poly(Gln) peptides with repeat lengths in the 15-20 residue range, despite their poor abilities to support spontaneous, self-nucleated aggregation, are capable of efficiently adding to an already-formed aggregate. We also find that morphologically small, finely divided aggregates are much more efficient at recruiting poly(Gln) peptides than are large aggregates, suggesting a possible explanation for why disease pathology does not always correlate with the observable NII burden. Together, these data are consistent with a model for disease pathology in which critical cellular proteins possessing poly(Gln) sequences of modest length become inactivated when they are recruited into aggregates of an expanded poly(Gln) protein. .COPYRGT. 2001 Academic Press.

=> chen s/au
L56 206 FILE AGRICOLA
L57 656 FILE BIOTECHNO
L58 299 FILE CONFSCI
L59 15 FILE HEALSAFE
'AU' IS NOT A VALID FIELD CODE
L60 0 FILE IMSDRUGCONF
L61 462 FILE LIFESCI
'AU' IS NOT A VALID FIELD CODE
L62 0 FILE MEDICONF
L63 999 FILE PASCAL

TOTAL FOR ALL FILES
L64 2637 CHEN S/AU

=> l64 and repeat and glutamine
L65 0 FILE AGRICOLA
L66 2 FILE BIOTECHNO
L67 0 FILE CONFSCI
L68 0 FILE HEALSAFE
L69 0 FILE IMSDRUGCONF

L70 2 FILE LIFESCI
L71 0 FILE MEDICONF
L72 0 FILE PASCAL

TOTAL FOR ALL FILES
L73 4 L64 AND REPEAT AND GLUTAMINE

=> dup rem
ENTER L# LIST OR (END):l73
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
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L74 2 DUP REM L73 (2 DUPLICATES REMOVED)

=> d l74 ibib abs total

L74 ANSWER 1 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2003:36183362 BIOTECHNO
TITLE: SCA7 knockin mice model human SCA7 and reveal gradual accumulation of mutant ataxin-7 in neurons and abnormalities in short-term plasticity
AUTHOR: Yoo S.-Y.; Pennesi M.E.; Weeber E.J.; Xu B.; Atkinson R.; **Chen S.**; Armstrong D.L.; Wu S.M.; Sweatt J.D.; Zoghbi H.Y.
CORPORATE SOURCE: H.Y. Zoghbi, Division of Neuroscience, Baylor College of Medicine, Houston, TX 77030, United States.
E-mail: hzoghbi@bcm.tmc.edu
SOURCE: Neuron, (06 FEB 2003), 37/3 (383-401), 60 reference(s)
CODEN: NERNET ISSN: 0896-6273
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:36183362 BIOTECHNO
AB We targeted 266 CAG **repeats** (a number that causes infantile-onset disease) into the mouse Sca7 locus to generate an authentic model of spinocerebellar ataxia type 7 (SCA7). These mice reproduced features of infantile SCA7 (ataxia, visual impairments, and premature death) and showed impaired short-term synaptic potentiation; downregulation of photoreceptor-specific genes, despite apparently normal CRX activity, led to shortening of photoreceptor outer segments. Wild-type ataxin-7 was barely detectable, as was mutant ataxin-7 in young animals; with increasing age, however, ataxin-7 staining became more pronounced. Neurons that appeared most vulnerable had relatively high levels of mutant ataxin-7; it is interesting, however, that marked dysfunction occurred in these neurons weeks prior to the appearance of nuclear inclusions. These data demonstrate that **glutamine** expansion stabilizes mutant ataxin-7, provide an explanation for selective neuronal vulnerability, and show that mutant ataxin-7 impairs posttetanic potentiation (PTP).

L74 ANSWER 2 OF 2 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 2002:34994493 BIOTECHNO
TITLE: Huntington's disease age-of-onset linked to polyglutamine aggregation nucleation
AUTHOR: **Chen S.**; Ferrone F.A.; Wetzel R.
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, Univ. of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (03 SEP 2002), 99/18

(11884-11889), 33 reference(s)
CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34994493 BIOTECHNO
AB In Huntington's Disease and related expanded CAG **repeat** diseases, a polyglutamine [poly(Gln)] sequence containing 36 **repeats** in the corresponding disease protein is benign, whereas a sequence with only 2-3 additional **glutamines** is associated with disease risk. Above this threshold range, longer **repeat** lengths are associated with earlier ages-of-onset. To investigate the biophysical basis of these effects, we studied the in vitro aggregation kinetics of a series of poly(Gln) peptides. We find that poly(Gln) peptides in solution at 37°C undergo a random coil to β-sheet transition with kinetics superimposable on their aggregation kinetics, suggesting the absence of soluble, β-sheet-rich intermediates in the aggregation process. Details of the time course of aggregate growth confirm that poly(Gln) aggregation occurs by nucleated growth polymerization. Surprisingly, however, and in contrast to conventional models of nucleated growth polymerization of proteins, we find that the aggregation nucleus is a monomer. That is, nucleation of poly(Gln) aggregation corresponds to an unfavorable protein folding reaction. Using parameters derived from the kinetic analysis, we estimate the difference in the free energy of nucleus formation between benign and pathological length poly(Gln)s to be less than 1 kcal/mol. We also use the kinetic parameters to calculate predicted aggregation curves for very low concentrations of poly(Gln) that might obtain in the cell. The **repeat** -length-dependent differences in predicted aggregation lag times are in the same range as the length-dependent age-of-onset differences in Huntington's disease, suggesting that the biophysics of poly(Gln) aggregation nucleation may play a major role in determining disease onset.

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                  STN Express with Discover!
 NEWS  4  OCT 28  KOREAPAT now available on STN
 NEWS  5  NOV 18  Current-awareness alerts, saved answer sets, and current
                  search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                  and SOLIDSTATE reloads
 NEWS  6  NOV 30  PHAR reloaded with additional data
 NEWS  7  DEC 01  LISA now available on STN
 NEWS  8  DEC 09  12 databases to be removed from STN on December 31, 2004
 NEWS  9  DEC 15  MEDLINE update schedule for December 2004

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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FULL ESTIMATED COST                                     0.21       0.21

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=> chen s/au
L1          911 FILE CAPLUS
L2          656 FILE BIOTECHNO
L3          530 FILE COMPENDEX
L4          155 FILE ANABSTR
L5            0 FILE CERAB
L6          421 FILE METADEX
L7            0 FILE USPATFULL

TOTAL FOR ALL FILES
L8         2673 CHEN S/AU

=> wetzel r/au
L9           69 FILE CAPLUS
L10          38 FILE BIOTECHNO
L11          17 FILE COMPENDEX
L12           5 FILE ANABSTR
L13           0 FILE CERAB
L14           3 FILE METADEX
L15           0 FILE USPATFULL

TOTAL FOR ALL FILES
L16         132 WETZEL R/AU

=> l8 and l16
L17           0 FILE CAPLUS
L18           4 FILE BIOTECHNO
L19           0 FILE COMPENDEX
L20           1 FILE ANABSTR
L21           0 FILE CERAB
L22           0 FILE METADEX
L23           0 FILE USPATFULL

TOTAL FOR ALL FILES
L24           5 L8 AND L16

=> d l24 ibib abs total

L24   ANSWER 1 OF 5  BIOTECHNO  COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER:        2002:34994493   BIOTECHNO
TITLE:                   Huntington's disease age-of-onset linked to
                         polyglutamine aggregation nucleation
AUTHOR:                  Chen S.; Ferrone F.A.; Wetzel R.
CORPORATE SOURCE:        R. Wetzel, Graduate School of Medicine, Univ. of
                         Tennessee Medical Center, 1924 Alcoa Highway,
                         Knoxville, TN 37920, United States.
                         E-mail: rwetzel@mc.utmck.edu
```

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (03 SEP 2002), 99/18 (11884-11889), 33 reference(s)
CODEN: PNASA6 ISSN: 0027-8424
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2002:34994493 BIOTECHNO
AB In Huntington's Disease and related expanded CAG repeat diseases, a polyglutamine [poly(Gln)] sequence containing 36 repeats in the corresponding disease protein is benign, whereas a sequence with only 2-3 additional glutamines is associated with disease risk. Above this threshold range, longer repeat lengths are associated with earlier ages-of-onset. To investigate the biophysical basis of these effects, we studied the in vitro aggregation kinetics of a series of poly(Gln) peptides. We find that poly(Gln) peptides in solution at 37°C undergo a random coil to β-sheet transition with kinetics superimposable on their aggregation kinetics, suggesting the absence of soluble, β-sheet-rich intermediates in the aggregation process. Details of the time course of aggregate growth confirm that poly(Gln) aggregation occurs by nucleated growth polymerization. Surprisingly, however, and in contrast to conventional models of nucleated growth polymerization of proteins, we find that the aggregation nucleus is a monomer. That is, nucleation of poly(Gln) aggregation corresponds to an unfavorable protein folding reaction. Using parameters derived from the kinetic analysis, we estimate the difference in the free energy of nucleus formation between benign and pathological length poly(Gln)s to be less than 1 kcal/mol. We also use the kinetic parameters to calculate predicted aggregation curves for very low concentrations of poly(Gln) that might obtain in the cell. The repeat-length-dependent differences in predicted aggregation lag times are in the same range as the length-dependent age-of-onset differences in Huntington's disease, suggesting that the biophysics of poly(Gln) aggregation nucleation may play a major role in determining disease onset.

L24 ANSWER 2 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32756978 BIOTECHNO
TITLE: A microtiter plate assay for polyglutamine aggregate extension
AUTHOR: Berthelier V.; Hamilton J.B.; **Chen S.**; **Wetzel R.**
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, R221, Univ. of Tennessee Medical Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.
SOURCE: Analytical Biochemistry, (15 AUG 2001), 295/2 (227-236), 43 reference(s)
CODEN: ANBCA2 ISSN: 0003-2697
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32756978 BIOTECHNO
AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded CAG repeat disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln

peptide. Europium-streptavidin complexation of the immobilized biotin, followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the assembly mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln length dependence. The assay also will be a valuable tool for screening and characterizing antiaggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism. .COPYRGT. 2001 Academic Press.

L24 ANSWER 3 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32735322 BIOTECHNO
TITLE: Polyglutamine aggregation behavior in vitro supports a recruitment mechanism of cytotoxicity
AUTHOR: **Chen S.**; Berthelier V.; Yang W.; **Wetzel R.**
CORPORATE SOURCE: R. Wetzel, Graduate School of Medicine, University of Tennessee Medical Ctr., 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Journal of Molecular Biology, (03 AUG 2001), 311/1 (173-182), 54 reference(s)
CODEN: JMOBAK ISSN: 0022-2836
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32735322 BIOTECHNO
AB In expanded CAG repeat diseases such as Huntington's disease, proteins containing polyglutamine (poly(Gln)) sequences with repeat lengths of about 37 residues or more are associated with development of both disease symptoms and neuronal intranuclear inclusions (NIIs). Disease physiology in animal and cellular models does not always correlate with NII formation, however, and the mechanism by which aggregate formation might lead to cytotoxicity is unknown. To help evaluate various possible mechanisms, we determined the biophysical properties of a series of simple poly(Gln) peptides. The circular dichroism spectra of poly(Gln) peptides with repeat lengths of tive, 15, 28 and 44 residues are all nearly identical and are consistent with a high degree of random coil structure, suggesting that the length-dependence of disease is not related to a conformational change in the monomeric states of expanded poly(Gln) sequences. In contrast, there is a dramatic increase in both the kinetics and the thermodynamic favorability of the spontaneous formation of ordered, amyloid-like aggregates for poly(Gln) peptides with repeat lengths of greater than 37 residues. At the same time, poly(Gln) peptides with repeat lengths in the 15-20 residue range, despite their poor abilities to support spontaneous, self-nucleated aggregation, are capable of efficiently adding to an already-formed aggregate. We also find that morphologically small, finely divided aggregates are much more efficient at recruiting poly(Gln) peptides than are large aggregates, suggesting a possible explanation for why disease pathology does not always correlate with the observable NII burden. Together, these data are consistent with a model for disease pathology in which critical cellular proteins possessing poly(Gln) sequences of modest length become inactivated when they are recruited into aggregates of an expanded poly(Gln) protein. .COPYRGT. 2001 Academic Press.

L24 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2001:32240515 BIOTECHNO
TITLE: Solubilization and disaggregation of polyglutamine peptides
AUTHOR: **Chen S.; Wetzel R.**

CORPORATE SOURCE: Dr. R. Wetzel, Graduate School of Medicine, R221 Univ. of Tennessee Med. Center, 1924 Alcoa Highway, Knoxville, TN 37920, United States.
E-mail: rwetzel@mc.utmck.edu
SOURCE: Protein Science, (2001), 10/4 (887-891), 16 reference(s)
CODEN: PRCIEI ISSN: 0961-8368
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2001:32240515 BIOTECHNO
AB A method is described for dissolving and disaggregating chemically synthesized polyglutamine peptides. Polyglutamine peptides longer than about Q.sub.2.sub.0 have been reported to be insoluble in water, but dissolution in - and evaporation from - a mixture of trifluoroacetic acid and hexafluoroisopropanol converts polyglutamine peptides up to at least Q.sub.4.sub.4 to a form readily soluble in aqueous buffers. This procedure also has a dramatic effect on peptides which appear to be completely soluble in water, by removing traces of aggregate that seed aggregation. The protocol makes possible solution studies - including in vitro aggregation experiments - on polyglutamine peptides with repeat lengths associated with increased risk of Huntington's Disease and other expanded CAG repeat diseases. It may also be useful in conducting reproducible, quantitative aggregation studies on other polypeptides.

L24 ANSWER 5 OF 5 ANABSTR
AB In connection the development of an assay for "extension-competent" or "seeding-competent" polyglutamine aggregates in tissue or serum, up to 5 ng portions of synthetic polyglutamine aggregates (SPA) were immobilized in microtitre-plate wells and incubated first with a standard amount of biotinylated SPA and then with Eu-streptavidin complex. The amount of Eu bound was measured by time-resolved fluorimetry and converted into the amount of biotinylated SPA on the basis of the association of seven Eu3+ with each molecule of streptavidin. The amount of biotinylated SPA bound varied linearly with the amount of SPA immobilized on the plate; the detection limit was 80 pg.

here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington**'s and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 3 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1999:29124713 BIOTECHNO
TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network
AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.
CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu
SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1999:29124713 BIOTECHNO
AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length** polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length** polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-**length** polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

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=> amyloid and (filament or aggregrate or assembly) and length and diameter
L35 1 FILE AGRICOLA
L36 4 FILE BIOTECHNO
L37 0 FILE CONFSCI
L38 0 FILE HEALSAFE
L39 0 FILE IMSDRUGCONF
L40 3 FILE LIFESCI
L41 0 FILE MEDICONF
L42 1 FILE PASCAL

TOTAL FOR ALL FILES
L43 9 AMYLOID AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH AND DIAMETER

=> dup rem
ENTER L# LIST OR (END):143
DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L43
L44 5 DUP REM L43 (4 DUPLICATES REMOVED)

=> d 144 ibib abs total

L44 ANSWER 1 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:37345999 BIOTECHNO
TITLE: Architecture of Ure2p Prion **Filaments**: The N-terminal domains form a central core fiber
AUTHOR: Baxa U.; Taylor K.L.; Wall J.S.; Simon M.N.; Cheng N.; Wickner R.B.; Steven A.C.
CORPORATE SOURCE: A.C. Steven, Bldg. 50, MSC 8025, 50 South Dr., Bethesda, MD 20892-8025, United States.
E-mail: Alasdair_Steven@nih.gov
SOURCE: Journal of Biological Chemistry, (31 OCT 2003), 278/44 (43717-43727), 46 reference(s)

CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37345999 BIOTECHNO
AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p determines its in vivo prion properties and in vitro **amyloid**-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diameter** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diameters** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning transmission electron microscopy (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

L44 ANSWER 2 OF 5 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2004) on STN DUPLICATE 1
ACCESSION NUMBER: 2002:50889 AGRICOLA
DOCUMENT NUMBER: IND23281705
TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein.
AUTHOR(S): Baxa, U.; Speransky, V.; Steven, A.C.; Wickner, R.B.
AVAILABILITY: DNAL (500 N21P)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Apr 16, 2002. Vol. 99, No. 8. p. 5253-5260
Publisher: Washington, D.C. : National Academy of Sciences,
CODEN: PNASA6; ISSN: 0027-8424
NOTE: Includes references
PUB. COUNTRY: District of Columbia; United States
DOCUMENT TYPE: Article; Conference
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English
AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diameters** increased with the mass of the appended enzyme. The

helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all beta-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

L44 ANSWER 3 OF 5 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 2
ACCESSION NUMBER: 1999:39603 LIFESCI
TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
AUTHOR: Taylor, K.L.; Cheng, Naiqian; Williams, R.W.; Steven, A.C.; Wickner, R.B.*
CORPORATE SOURCE: Lab. Biochem. and Genet., Natl. Inst. Health, Bethesda, MD 20892-0830, USA; E-mail: wickner@helix.nih.gov
SOURCE: Science (Washington) [Science (Wash.)], (19990226) vol. 283, no. 5406, pp. 1339-1343.
ISSN: 0036-8075.
DOCUMENT TYPE: Journal
FILE SEGMENT: K; V
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The [URE3] non-Mendelian genetic element of Saccharomyces cerevisiae is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p super(1-65) were shown to polymerize to form **filaments** 40 to 45 angstroms in **diameter** with more than 60 percent beta sheet. Ure2p specifically induced full-**length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in extracts of [URE3] strains, these 180- to 220-angstrom-**diameter filaments** were protease resistant. The Ure2p super(1-65)-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular **filaments**. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].

L44 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21180842 BIOTECHNO
TITLE: Morphology and antibody recognition of synthetic β- **amyloid** peptides
AUTHOR: Fraser P.E.; Duffy L.K.; O'Malley M.B.; Nguyen J.; Inouye H.; Kirschner D.A.
CORPORATE SOURCE: Neurology Research, Children's Hospital, Enders 2, 320 Longwood Ave.,Boston, MA 02115, United States.
SOURCE: Journal of Neuroscience Research, (1991), 28/4 (474-485)
CODEN: JNREDK ISSN: 0360-4012
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21180842 BIOTECHNO
AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β-**amyloid** protein (β-AP), we investigated the ability of peptides sharing sequences with β-AP to form fibrils in vitro and to recognize anti-β- **amyloid** antisera. The peptides, which

were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β-AP. Electron microscopy of negative-stained or thin-sectioned preparations revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diameters** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diameters** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1,100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diameter**. When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross-β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β-(1-28) was highly reactive in an inhibition-ELISA assay to β-(6-25) and β-(1-38), but not to β-(22-35), and immunostained β-(1-40) on Western blots. These studies show that the β-(6-25), β-(1-38) and β-(1-40) peptides can assemble into cross-β fibrils that retain epitopes characteristic of AD **amyloid**.

L44 ANSWER 5 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1985:15068440 BIOTECHNO
TITLE: Identification of prion **amyloid** **filaments** in scrapie-infected brain
AUTHOR: DeArmond S.J.; McKinley M.P.; Barry R.A.; et al.
CORPORATE SOURCE: Department of Pathology, University of California, San Francisco, CA 94143, United States.
SOURCE: Cell, (1985), 41/1 (221-235)
CODEN: CELLB5
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English

AN 1985:15068440 BIOTECHNO
AB Extracellular collections of abnormal **filaments** composed of prion proteins have been identified in the brains of scrapie-infected hamsters using immuno-electron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, and determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

=> file .jacob

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	19.73	76.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE ENTRY: 0.00 TOTAL SESSION: -1.40

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FILE 'MEDLINE' ENTERED AT 15:31:45 ON 16 DEC 2004

FILE 'EMBASE' ENTERED AT 15:31:45 ON 16 DEC 2004

FILE 'USPATFULL' ENTERED AT 15:31:45 ON 16 DEC 2004

=> (cag repeat) and (huntington or drpla or ataxin) and (filament or aggregrate or assembly) and length
L45 2 FILE CAPLUS
L46 4 FILE BIOSIS
L47 1 FILE MEDLINE
L48 2 FILE EMBASE
L49 50 FILE USPATFULL

TOTAL FOR ALL FILES
L50 59 (CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH

=> dup rem
ENTER L# LIST OR (END):l45-l48
PROCESSING COMPLETED FOR L45
PROCESSING COMPLETED FOR L46
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L48
L51 5 DUP REM L45-L48 (4 DUPLICATES REMOVED)

=> d l51 ibib abs total

L51 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:716876 CAPLUS
DOCUMENT NUMBER: 139:287912
TITLE: **Ataxin**-3 interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis
AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran
CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA
SOURCE: Molecular and Cellular Biology (2003), 23(18), 6469-6483
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin**-3. We investigated whether **ataxin**-3 is a

proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin**-3 interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin**-3 assocs. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin**-3 is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:278678 BIOSIS
DOCUMENT NUMBER: PREV200200278678
TITLE: Remedy for **CAG repeat** expansion diseases.
AUTHOR(S): Tsuji, Shoji [Inventor, Reprint author]
CORPORATE SOURCE: Niigata, Japan
ASSIGNEE: Niigata University, Japan
PATENT INFORMATION: US 6355690 March 12, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 12, 2002) Vol. 1256, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB To elucidate the molecular mechanisms of "gain of toxic function" of expanded polyglutamine stretches in **CAG repeat** expansion diseases, the inventors established an expression system of full-**length** and truncated cDNAs for dentatorubral-pallidoluysian atrophy (**DRPLA**) and found that truncated **DRPLA** proteins containing the expanded polyglutamine stretch, but not the full-**length** protein, form peri- and intra-nuclear aggregates consisting of **filaments** and concomitant apoptosis. The apoptotic cell death was partially suppressed by transglutaminase inhibitors, cystamine and monodansyl cadaverine, raising the possibility of involvement of transglutaminase reaction. The results may provide a potential basis for the development of therapeutic measures for **CAG repeat** expansion diseases.

L51 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelier, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzel, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399 CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the

cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington**'s disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β-sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington**'s and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:433998 BIOSIS
DOCUMENT NUMBER: PREV200100433998
TITLE: A microtiter plate assay for polyglutamine aggregate extension.
AUTHOR(S): Berthelier, Valerie; Hamilton, J. Bradley; Chen, Songming; Wetzel, Ronald [Reprint author]
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, R221, Knoxville, TN, 37920, USA
SOURCE: Analytical Biochemistry, (August 15, 2001) Vol. 295, No. 2, pp. 227-236. print.
CODEN: ANBCA2. ISSN: 0003-2697.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded **CAG repeat** disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln peptide. Europium-streptavidin complexation of the immobilized biotin,

followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the **assembly** mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln **length** dependence. The assay also will be a valuable tool for screening and characterizing anti-aggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism.

L51 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
DUPLICATE 2
ACCESSION NUMBER: 1999:180905 BIOSIS
DOCUMENT NUMBER: PREV199900180905
TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network.
AUTHOR(S): Nagai, Yoshitaka; Onodera, Osamu; Chun, Jerold; Strittmatter, Warren J.; Burke, James R. [Reprint author]
CORPORATE SOURCE: Department of Medicine (Neurology), Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Experimental Neurology, (Feb., 1999) Vol. 155, No. 2, pp. 195-203. print.
CODEN: EXNEAC. ISSN: 0014-4886.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease-producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length** polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length** polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-**length** polyglutamine proteins coisolated 68-kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

=> amyloid and (filament or aggregrate or assembly) and length and diameter
L52 11 FILE CAPLUS
L53 8 FILE BIOSIS
L54 9 FILE MEDLINE
L55 10 FILE EMBASE
L56 793 FILE USPATFULL

TOTAL FOR ALL FILES
L57 831 AMYLOID AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH AND DIAMETER

=> dup rem
ENTER L# LIST OR (END):152-155
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PROCESSING COMPLETED FOR L53

PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L55
L58 16 DUP REM L52-L55 (22 DUPLICATES REMOVED)

=> d l58 ibib abs total

L58 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:495393 CAPLUS
DOCUMENT NUMBER: 141:201912
TITLE: The formation of straight and twisted **filaments** from short tau peptides
AUTHOR(S): Goux, Warren J.; Kopplin, Lauren; Nguyen, Anh D.; Leak, Kathryn; Rutkofsky, Marni; Shanmuganandam, Vasanthi D.; Sharma, Deepak; Inouye, Hideyo; Kirschner, Daniel A.
CORPORATE SOURCE: Department of Chemistry, the University of Texas at Dallas, Richardson, TX, 75083-0688, USA
SOURCE: Journal of Biological Chemistry (2004), 279(26), 26868-26875
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied fibril formation in a family of peptides based on PHF6 (VQIVYK), a short peptide segment found in the microtubule binding region of tau protein. N-Acetylated peptides AcVYK-amide (AcVYK), AcIVYK-amide (AcPHF4), AcQIVYK-amide (AcPHF5), and AcV-QIVYK-amide (AcPHF6) rapidly formed straight **filaments** in the presence of 0.15 M NaCl, each composed of two laterally aligned protofilaments .apprx.5 nm in width. X-ray fiber diffraction showed the omnipresent sharp 4.7-Å reflection indicating that the scattering objects are likely elongated along the hydrogen-bonding direction in a cross-β conformation, and Fourier transform IR suggested the peptide chains were in a parallel (AcVYK, AcPHF6) or antiparallel (AcPHF4, AcPHF5) β-sheet configuration. The dipeptide N-acetyl-YK-amide (AcYK) formed globular structures .apprx.200 nm to 1 μm in **diam**. The polymerization rate, as measured by thioflavin S binding, increased with the **length** of the peptide going from AcYK → AcPHF6, and peptides that aggregated most rapidly displayed CD spectra consistent with β-sheet structure. There was a 3-fold decrease in rate when Val was substituted for Ile or Gln, nearly a 10-fold decrease when Ala was substituted for Tyr, and an increase in polymerization rate when Glu was substituted for Lys. Twisted **filaments**, composed of four laterally aligned protofilaments (9-19 nm width, .apprx.90 nm half-periodicity), were formed by mixing AcPHF6 with AcVYK. Taken together these results suggest that the core of PHF6 is localized at VYK, and the interaction between small amphiphilic segments of tau may initiate nucleation and lead to **filaments** displaying paired helical **filament** morphol.
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:160995 BIOSIS
DOCUMENT NUMBER: PREV200400164922
TITLE: Formation of **amyloid** from superoxide dismutase.
AUTHOR(S): Oztug, Zeynep [Reprint Author]; Padua, Shelby [Reprint Author]; Downes, Sean [Reprint Author]; Cohlberg, Jeffrey A. [Reprint Author]; Rodriguez, Jorge; Doucette, Peter; Valentine, Joan S.
CORPORATE SOURCE: Dept of Chemistry and Biochemistry, California State University, Long Beach, Long Beach, CA, USA
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

504a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004

AB Mutations in copper-zinc superoxide dismutase (SOD) are the cause of 20 percent of the cases of familial amyotrophic lateral sclerosis (FALS). Insoluble deposits containing SOD are found in motor neurons of FALS patients, some of which are reactive with the **amyloid**-specific dye thioflavin S. It has been proposed that the mutations cause the disease by increasing the tendency of SOD to aggregate. Furthermore, certain SOD crystal structures show linear arrays of SOD dimers similar to **amyloid filaments**. Therefore, conditions were sought under which SOD forms **amyloid**. Protein solutions were agitated at 37C in the presence of thioflavin T, and **amyloid** formation was detected by monitoring fluorescence with a microplate reader. Wild-type SOD formed **amyloid** at pH 3 and 0.5-2 M guanidine hydrochloride, with an optimum of about 1 M guanidine. The kinetics showed a lag phase of variable **length**, typically about 24 hr, followed by a rise in fluorescence over a period of a few hours. Incubation of the product with Congo Red produced a shift in the absorbance peak from 510 nm to 542 nm. Transmission electron microscopy revealed straight **filaments** with **diameters** of about 10 nm, often appearing as bundles up to 50 nm in **diameter**. Apo-SOD did not form **amyloid** under these conditions. Various FALS-related mutant SODs also formed **amyloid filaments** at acidic pH and low concentrations of guanidine. For some of the mutants less acidic conditions were required to promote **amyloid** formation. Under some conditions, mutant SODs formed **amyloid** only when seeded by preexisting **amyloid**, while seeding appeared to have no effect with other samples. 30% acetonitrile can substitute for guanidine hydrochloride in promoting **amyloid** formation. The results may be relevant to the aggregation of SOD which occurs in motor neurons in FALS.

L58 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:660806 CAPLUS
TITLE: Nanostructure of β-sheet fibrils constructed by unfolded β-hairpin peptide self- **assembly**
AUTHOR(S): Lamm, Matthew S.; Rajagopal, Karthikan; Schneider, Joel P.; Pochan, Darrin J.
CORPORATE SOURCE: Department of Materials Science and Engineering, University of Delaware, Newark, DE, 19716, USA
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), POLY-345. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB A 20-residue peptide consisting of alternating valine and lysine residues flanking a tripeptide turn sequence has been shown to self-assemble via differing pathways into dramatically different materials, depending on the primary structure of the turn sequence. Under appropriate solution conditions, peptides with type II' turn sequences intramolecularly fold leading to β-sheet rich, reversible hydrogelation. Alternatively, almost identical peptides, differing only in turn sequence that strongly disfavors intramol. folding, adopt an extended β-sheet conformation and irreversibly assemble into β- **amyloid**-like, prion-like

fibrillar structures. The resulting fibrillar structures are analyzed using transmission electron microscopy, atomic force microscopy and x-ray diffraction; an untwisted, un-branched morphol. is observed characterized by lateral **assembly** of .apprx.2.5nm **diam.** **filaments** and up to microns in **length**. Lateral association of **filaments** produced fibril widths of 100nm or more. Each fibril has an exact height of .apprx.6.7nm suggesting that each peptide is in an extended conformation with the peptide backbone orthogonal to both the fibril axis and the direction of lamination.

L58 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:850847 CAPLUS
DOCUMENT NUMBER: 140:2085
TITLE: Architecture of Ure2p Prion **Filaments**: the N-terminal domains form a central core fiber
AUTHOR(S): Baxa, Ulrich; Taylor, Kimberly L.; Wall, Joseph S.; Simon, Martha N.; Cheng, Naiqian; Wickner, Reed B.; Steven, Alasdair C.
CORPORATE SOURCE: Lab. Struct. Biol., Natl. Inst. Arthritis, Musculoskeletal, and Skin Dis., Natl. Inst. Health, Bethesea, MD, 20892, USA
SOURCE: Journal of Biological Chemistry (2003), 278(44), 43717-43727
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p dets. its in vivo prion properties and in vitro **amyloid**-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diam.** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diams**. of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning TEM (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:72748 CAPLUS
DOCUMENT NUMBER: 136:146104
TITLE: Human stress genes identified using DNA microarrays
INVENTOR(S): Chenchik, Alex; Lukashev, Matvey E.
PATENT ASSIGNEE(S): Clontech, USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 441,920.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002009730	A1	20020124	US 2001-782909	20010213
PRIORITY APPLN. INFO.:			US 1998-222256 B2	19981228
			US 1999-440305 B2	19991117
			US 1999-441920 A2	19991117

AB Human stress arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe composition of unique polynucleotides corresponding to a human stress gene. The average **length** of the polynucleotide probes is between 50 to 1000 nucleotides. The d. of the spots on the array did not exceed 400/cm2 and the spots had a **diam**. ranging between 10 to 5000 μm. Furthermore, the number of polynucleotide probe spots on the array ranged between 50 to 2000 nucleotides. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of human stress genes. 236 Different human stress genes were identified using this approach.

L58 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:316601 CAPLUS
DOCUMENT NUMBER: 137:45099
TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein
AUTHOR(S): Baxa, Ulrich; Speransky, Vladislav; Steven, Alasdair C.; Wickner, Reed B.
CORPORATE SOURCE: Laboratories of Structural Biology, National Institute of Arthritis, Musculoskeletal Diseases, and Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(8), 5253-5260
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich N-terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diams**. increased with the mass of the appended enzyme. The helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all β-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:703452 CAPLUS
DOCUMENT NUMBER: 138:2785
TITLE: Examining the structure of the mature **amyloid** fibril
AUTHOR(S): Makin, O. S.; Serpell, L. C.
CORPORATE SOURCE: Structural Medicine Unit, Cambridge Institute for Medical Research, Cambridge, CB2 2XY, UK
SOURCE: Biochemical Society Transactions (2002), 30(4), 521-525
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The pathogenesis of the group of diseases known collectively as the amyloidoses is characterized by the deposition of insol. **amyloid** fibrils. These are straight, unbranching structures about 70-120 Å (1 Å = 0.1 nm) in **diam.** and of indeterminate **length** formed by the self-**assembly** of a diverse group of normally soluble proteins. Knowledge of the structure of these fibrils is necessary for the understanding of their abnormal **assembly** and deposition, possibly leading to the rational design of therapeutic agents for their prevention or disaggregation. Structural elucidation is impeded by fibril insoly. and inability to crystallize, thus preventing the use of x-ray crystallog. and solution NMR. CD, Fourier-transform IR spectroscopy and light scattering have been used in the study of the mechanism of fibril formation. This review concs. on the structural information about the final, mature fibril and in particular the complementary techniques of cryo-electron microscopy, solid-state NMR and x-ray fiber diffraction.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001241576 EMBASE
TITLE: Yeast prions act as genes composed of self-propagating protein **amyloids**.
AUTHOR: Wickner R.B.; Taylor K.L.; Edskes H.K.; Maddelein M.-L.; Moriyama H.; Tibor Roberts B.
CORPORATE SOURCE: R.B. Wickner, Laboratory of Biochemistry, Natl. Inst. Diab. Digest./Kid. Dis., National Institutes of Health, Bethesda, MD 20892, United States
SOURCE: Advances in Protein Chemistry, (2001) 57/- (313-334).
Refs: 71
ISSN: 0065-3233 CODEN: APCHA2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We proposed genetic properties by which prions can be recognized among infectious elements. This indicated that [URE3] and [PSI], two nonchromosomal genetic elements of yeast, were prions (infectious altered forms) of Ure2p and Sup35p, respectively. Overexpression of Ure2p leads to the de novo appearance of the [URE3] prion, and the N-terminal 65-80 residues (the prion domain) are specifically responsible for this prion-inducing activity. The prion domain is sufficient to propagate [URE3] and is necessary for a Ure2p molecule to be affected by [URE3]. The remaining C-terminal residues 81-354 are responsible for nitrogen catabolite repression, the normal function of Ure2p. Ure2p is protease-resistant specifically in extracts of [URE3] strains and is

aggregated in vivo specifically in such strains. The chemically synthesized Ure2p prion domain (Ure2p(1-65)) spontaneously forms classic **amyloid filaments** (50 A **diameter**) in vitro, and specifically induces the native full **length** Ure2p to form a 1:1 **amyloid** cofilament (200 A). These **amyloid** cofilaments can prime amyoid **filament** formation by an excess of native Ure2p. The features of the in vitro **amyloid** propagation reaction appear to reproduce the in vivo properties of [URE3] prion propagation. This system may be useful for detecting new prions, finding **amyloid**-inducing and **amyloid**-curing agents, and determining the cellular components that affect the initiation and propagation of infectious **amyloids**. The [Het-s] prion was found in the filamentous fungus Podospora anserina by similar genetic tests to those we used for [URE3] and [PSI]. [Het-s] is necessary for a normal function of Podospora cells, heterokaryon incompatibility. This suggests that other normal cellular functions may involve a prion-like mechanism.

L58 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:80946 BIOSIS
DOCUMENT NUMBER: PREV200100080946
TITLE: A de novo designed helix-turn-helix peptide forms nontoxic **amyloid** fibrils.
AUTHOR(S): Fezoui, Y. [Reprint author]; Hartley, D. M.; Walsh, D. M.; Selkoe, D. J.; Osterhout, J. J.; Teplow, D. B.
CORPORATE SOURCE: Brigham and Women's Hospital, Boston, MA, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-299.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

AB During fibrillogenesis studies of the **amyloid** beta-protein (Abeta), we sought a non-amyloidogenic "negative control" peptide. Prior work suggested that alphatalpha, a de novo designed, monomeric, 38-residue alpha-helix-turn-alpha-helix peptide would be ideal. alphatalpha was developed as a model for the study of protein folding intermediates and has a protein-like sequence and a stable tertiary structure. At pH 3.6 and pH 10.5, alphatalpha showed no aggregation after 8 weeks of incubation at 37degreeC. Surprisingly, at neutral pH, alphatalpha formed fibrils after 2 days of incubation at 37degreeC. Negative staining and electron microscopy revealed non-branching fibril **assemblies** 6-10 nm in width, which varied in **length** from 200 to 1200 nm. These **assemblies** were composed of two or more **filaments**, each 3-3.5 nm in **diameter**, and had the appearance of narrow ribbons. These types of structures also formed during the fibrillogenesis of Abeta and of the islet **amyloid** polypeptide (IAPP), however the rope-like, bifilar structures often seen in fibrils of Abeta and IAPP were not observed in alphatalpha fibrils. In common with the fibrillogenesis of Abeta and IAPP, alphatalpha fibril **assembly** involved an alpha-helixfwdarwbeta-sheet conformational change and the development of Congo red binding capacity. The shared morphologic, spectroscopic, and tinctorial properties of alphatalpha, Abeta, and IAPP fibrils suggested that alphatalpha fibrils might also share cytotoxic activity. However, alphatalpha fibrils were not toxic to cultured rat primary cortical neurons or to PC12 cells. These results suggest that the potential to form fibrils is not limited to those proteins associated with amyloidoses and that fibril formation alone is not predictive of cytotoxic activity.

L58 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1999:164136 CAPLUS
DOCUMENT NUMBER: 130:322093
TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
AUTHOR(S): Taylor, Kimberly L.; Cheng, Naiqian; Williams, Robert W.; Steven, Alasdair C.; Wickner, Reed B.
CORPORATE SOURCE: Laboratory of Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0830, USA
SOURCE: Science (Washington, D. C.) (1999), 283(5406), 1339-1343
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The [URE3] non-Mendelian genetic element of Saccharomyces cerevisiae is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p1-65 were shown to polymerize to form **filaments** 40 to 45 angstroms in **diam**. with more than 60 % β sheet. Ure2p1-65 specifically induced full- **length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in exts. of [URE3] strains, these 180- to 220-angstrom-**diam**. **filaments** were protease resistant. The Ure2p1-65-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular **filaments**. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97327024 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9183822
TITLE: As you like it.
AUTHOR: Ghadially F N
CORPORATE SOURCE: Department of Laboratory Medicine, Ottawa Civic Hospital, Ontario, Canada.
SOURCE: Ultrastructural pathology, (1997 May-Jun) 21 (3) 211-26.
Ref: 38
Journal code: 8002867. ISSN: 0191-3123.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19990129
Entered Medline: 19970724
AB I have developed something of a reputation for criticizing freely and frequently at our meetings and in my writings. You say you like this and find it useful and entertaining. As you like it, you are welcome to more of it. My comments and criticisms are presented under the following headings: (1) criticize at your peril; (2) how it all started (unjustly accused!); (3) abbreviations (a source of perennial aggravation, confusion, and waste of time); (4) mysterious bodies in mesotheliomas; (5) call a crystal a "crystal," not a "crystalloid"; (6) electron microscopy-a study of osmium artifacts; (7) **length**-to-**diameter** ratio of microvilli (mission impossible); (8) lamellar bodies (a popular

but debased term); (9) **amyloid filaments**, not fibers; (10) **filaments** and microtubules do not branch; (11) there is no such thing as pseudomelanosis; (12) botched histochemistry (just about every gastrointestinal tract pigment was misdiagnosed by histochemistry); (13) intranuclear Russell bodies, not "Dutcher bodies"; and (14) nuclear pores and virus-like particles (a new development in an old farce).

L58 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1991:245425 CAPLUS
DOCUMENT NUMBER: 114:245425
TITLE: Morphology and antibody recognition of synthetic β- **amyloid** peptides
AUTHOR(S): Fraser, P. E.; Duffy, L. K.; O'Malley, M. B.; Nguyen, J.; Inouye, H.; Kirschner, D. A.
CORPORATE SOURCE: Neurol. Res., Child. Hosp., Boston, MA, 02115, USA
SOURCE: Journal of Neuroscience Research (1991), 28(4), 474-85
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β- **amyloid** protein (β-AP), this study investigated the ability of peptides sharing sequences with β-AP to form fibrils in vitro and to recognize anti-β- **amyloid** antisera. The peptides, which were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β-AP. Electron microscopy of neg.-stained or thin-sectioned prepns. revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diams**. of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diams**. of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diam**. When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross-β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β-(1-28) was highly reactive in an inhibition-ELISA assay to β-(6-25) and β-(1-38), but not to β-(22-35), and immunostained β-(1-40) on Western blots. These studies show that the β-(6-25), β-(1-38) and β-(1-40) peptides can assemble into cross-β fibrils that retain epitopes characteristic of AD **amyloid**.

L58 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:405318 CAPLUS
DOCUMENT NUMBER: 111:5318
TITLE: Comparison of **amyloid** from Alzheimer's disease with synthetic peptide
AUTHOR(S): Duffy, Lawrence K.; Kirschner, Daniel A.; Joachim, Catharine L.; Sinclair, Alison; Inouye, Hideyo; Selkoe, Dennis J.
CORPORATE SOURCE: Cent. Neurol. dis., Brigham and Women's Hosp., Boston, MA, USA
SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988), Meeting Date 1987, 604-7. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.

CODEN: 56MDA6
DOCUMENT TYPE: Conference
LANGUAGE: English
AB X-ray patterns from partially dried, oriented pellets of β-peptide show characteristic cross β-spacings: a strong meriodional arc at 4.76 Å and a diffuse equatorial arc at 10.6 Å. These spacings and the other ones observed at wide angles are similar to those reported for β-keratin. The series of small angle intensity maximum along the equator indicate the fibril is tubular with a **diam**. of 71 Å and that the wall is composed of 2 or 3 cross β-pleated sheets. When the synthetic β-peptide **length** was increased to 45 amino acids to encompass some of the proposed membrane spanning region, it became very insol. and 88% formic acid had to be used initially to solubilize it. X-ray patterns from this peptide (β-45) in the presence of 25% trifluoroacetic acid showed β-pleated sheet spacings at about 11 Å and 4.7 Å spacings; similar but weaker patterns have been recorded for cerebral vascular **amyloid**. An analog peptide, β-28 (16-Ala) was synthesized and produced polymorphic structures whose **assemblies** were 5 or 6 β-sheets instead of 2 or 3. There was a differential inhibition loss of 20% of binding of antibody to β-28-coated plates with β-28 (16-Ala) suggesting that Lys-16 is exposed in the **amyloid** fibrils and that alanine at that position promotes intersheet stacking. Thus, the Alzheimer's disease **amyloid** behavior can be examined using synthetic peptides. A preliminary model of an **amyloid** peptide fibril is presented. Further studies using peptide analogs can be used to test this model.

L58 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1988:201098 CAPLUS
DOCUMENT NUMBER: 108:201098
TITLE: A close ultrastructural relationship between sulfated proteoglycans and AA **amyloid** fibrils
AUTHOR(S): Snow, Alan David; Willmer, Jonathan; Kisilevsky, Robert
CORPORATE SOURCE: Dep. Pathol., Queen's Univ., Kingston, ON, Can.
SOURCE: Laboratory Investigation (1987), 57(6), 687-98
CODEN: LAINAW; ISSN: 0023-6837
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two cationic reagents, ruthenium red (RR) and cuprolinic blue (CB), were used to assess the morphol. and structural relationship between sulfated proteoglycans and AA **amyloid** fibrils in amyloidotic spleen and liver, and in isolated fibril prepns. Amyloidotic tissue fixed in the presence of RR showed RR granules, measuring 15 to 25 nm in **diam**., over areas of electron-dense fibrils. In isolated fibril prepns., RR granules were specifically localized on **amyloid** fibrils. Amyloidotic tissue fixed in the presence of CB at 0.1M and 0.7M MgCl2 showed both granule and filamentous (50 to 90 nm in **length**) staining only over areas of **amyloid** fibrils. This same staining localization was also seen in isolated fibril prepns. The RR and CB granules and **filaments**, are believed to represent proteoglycan monomers with the glycosaminoglycan chains collapsed onto the protein core. The persistent CB staining at 0.7M MgCl2 suggested that highly sulfated proteoglycans were present. The glycosaminoglycan moiety has previously been identified as heparin/heparan sulfate. The intimate structural relationship between sulfated proteoglycans and AA **amyloid** fibrils, both in situ and in isolated fibril prepns., further suggests that these highly neg. charged mols. may have an important role in the pathogenesis of amyloidosis. Several pathogenetic scenarios are suggested.

L58 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1987:134807 CAPLUS
DOCUMENT NUMBER: 106:134807

TITLE: On the biology of prions
AUTHOR(S): Prusiner, S. B.; Gabizon, R.; McKinley, M. P.
CORPORATE SOURCE: Dep. Neurol., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Acta Neuropathologica (1987), 72(4), 299-314
CODEN: ANPTAL; ISSN: 0001-6322
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 147 refs. Prions cause scrapie and Creutzfeldt-Jakob disease (CJD); these infectious pathogens are composed largely, if not entirely, of protein mols. No prion-specific polynucleotide has been identified. Purified prepns. of scrapie prions contain high titers (≥109.5 ID50/mL), one protein (PrP 27-30), and **amyloid** rods (10-20 nm in **diam**. + 100-200 nm in **length**). Considerable evidence indicates that PrP 27-30 is required for and inseparable from scrapie infectivity. PrP 27-30 is encoded by a cellular gene and is derived from a larger protein, denoted PrPSc or PrP 33-35Sc, by protease digestion. A cellular isoform, designated PrPC or PprP 33-35C, is encoded by the same gene as PrPSc, and both proteins appear to be translated from the same 2.1 kb mRNA. Monoclonal antibodies to PrP 27-30, as well as antisera to PrP synthetic peptides, specifically react with both PrPC and PrPSc, establishing their relatedness. PrPC is digested by proteinase K, while PrPSc is converted to PrP 27-30 under the same conditions. Prion proteins are synthesized with signal peptides and are integrated into membranes. Detergent extraction of microsomal membranes isolated from scrapie-infected hamster brains solubilizes PrPC but induces PrPSc to polymerize into **amyloid** rods. This procedure allows separation of the two prion protein isoforms and the demonstration that PrPSc accumulates during scrapie infection, while the level of PrPC does not change. The prion **amyloid** rods generated by detergent extraction are identical morphol., except for **length**, to extracellular collections of prion **amyloid filaments** which form plaques in scrapie- and CJD-infected brains. The prion **amyloid** plaques stain with antibodies to PrP 27-30 and PrP peptides. PrP 33-35C does not accumulate in the extracellular space. Prion rods composed of PrP 27-30 can be dissociated into phospholipid vesicles with full retention of scrapie infectivity. The murine PrP gene (Prn-p) is linked to the Prn-i gene which controls the **length** of the scrapie incubation period. Prolonged incubation times are a cardinal feature of scrapie and CJD. While the central role of PrPSc in scrapie pathogenesis is well established, the chemical as well as conformational differences between PrPC and PrPSc are unknown but probably arise from post-translational modifications.

L58 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 9
ACCESSION NUMBER: 1985:380799 BIOSIS
DOCUMENT NUMBER: PREV198580050791; BA80:50791
TITLE: IDENTIFICATION OF PRION **AMYLOID FILAMENTS** IN SCRAPIE-INFECTED BRAIN.
AUTHOR(S): DEARMOND S J [Reprint author]; MCKINLEY M P; BARRY R A; BRAUNFELD M B; MCCOLLOCH J R; PRUSINER S B
CORPORATE SOURCE: DEP OF PATHOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIF 94143, USA
SOURCE: Cell, (1985) Vol. 41, No. 1, pp. 221-236.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Extracellular collections of abnormal **filaments** composed of prion proteins were identified in the brains of scrapie-infected hamsters using immunoelectron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted

appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, as determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

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                MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
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L2 0 FILE BIOTECHNO
L3 0 FILE CONFSCI
L4 0 FILE HEALSAFE
L5 0 FILE IMSDRUGCONF
L6 0 FILE LIFESCI
L7 0 FILE MEDICONF
L8 0 FILE PASCAL

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L9 0 (CAG REPEAT) AND AGGREGRATE AND LENGTH AND DIAMETER

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FILE 'ANABSTR' ENTERED AT 15:20:24 ON 16 DEC 2004

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L13 0 FILE ANABSTR
L14 0 FILE CERAB
L15 0 FILE METADEX
L16 0 FILE USPATFULL

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L17 0 (CAG REPEAT) AND AGGREGRATE AND LENGTH AND DIAMETER

=> glutamine and aggregrate and length and diameter
L18 0 FILE CAPLUS
L19 0 FILE BIOTECHNO
L20 0 FILE COMPENDEX
L21 0 FILE ANABSTR
L22 0 FILE CERAB
L23 0 FILE METADEX
L24 1 FILE USPATFULL

TOTAL FOR ALL FILES
L25 1 GLUTAMINE AND AGGREGRATE AND LENGTH AND DIAMETER

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L26 2 FILE CAPLUS
L27 1 FILE BIOTECHNO
L28 0 FILE COMPENDEX
L29 0 FILE ANABSTR
L30 0 FILE CERAB
L31 0 FILE METADEX
L32 50 FILE USPATFULL

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L34 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:716876 CAPLUS
DOCUMENT NUMBER: 139:287912
TITLE: **Ataxin**-3 interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis
AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran
CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA
SOURCE: Molecular and Cellular Biology (2003), 23(18),

6469-6483
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin**-3. We investigated whether **ataxin**-3 is a proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin**-3 interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin**-3 assocs. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin**-3 is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelier, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzel, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington**'s disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β-sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied

here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington**'s and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L34 ANSWER 3 OF 3 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1999:29124713 BIOTECHNO

TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network

AUTHOR: Nagai Y.; Onodera O.; Chun J.; Strittmatter W.J.; Burke J.R.

CORPORATE SOURCE: J.R. Burke, Department of Medicine (Neurology), Deane Laboratory, Duke University Medical Center, Durham, NC 27710, United States.
E-mail: james.burke@duke.edu

SOURCE: Experimental Neurology, (1999), 155/2 (195-203), 50 reference(s)
CODEN: EXNEAC ISSN: 0014-4886

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

AN 1999:29124713 BIOTECHNO

AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease- producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length** polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length** polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-**length** polyglutamine proteins coisolated 68- kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

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=> file .meeting
'EVENTLINE' IS NOT A VALID FILE NAME
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FILE 'AGRICOLA' ENTERED AT 15:24:54 ON 16 DEC 2004

FILE 'BIOTECHNO' ENTERED AT 15:24:54 ON 16 DEC 2004

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FILE 'PASCAL' ENTERED AT 15:24:54 ON 16 DEC 2004

=> amyloid and (filament or aggregrate or assembly) and length and diameter
L35 1 FILE AGRICOLA
L36 4 FILE BIOTECHNO
L37 0 FILE CONFSCI
L38 0 FILE HEALSAFE
L39 0 FILE IMSDRUGCONF
L40 3 FILE LIFESCI
L41 0 FILE MEDICONF
L42 1 FILE PASCAL

TOTAL FOR ALL FILES
L43 9 AMYLOID AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH AND DIAMETER

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DUPLICATE IS NOT AVAILABLE IN 'IMSDRUGCONF, MEDICONF'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
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L44 5 DUP REM L43 (4 DUPLICATES REMOVED)

=> d l44 ibib abs total

L44 ANSWER 1 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 2003:37345999 BIOTECHNO
TITLE: Architecture of Ure2p Prion **Filaments**: The N-terminal domains form a central core fiber
AUTHOR: Baxa U.; Taylor K.L.; Wall J.S.; Simon M.N.; Cheng N.; Wickner R.B.; Steven A.C.
CORPORATE SOURCE: A.C. Steven, Bldg. 50, MSC 8025, 50 South Dr., Bethesda, MD 20892-8025, United States.
E-mail: Alasdair_Steven@nih.gov
SOURCE: Journal of Biological Chemistry, (31 OCT 2003), 278/44 (43717-43727), 46 reference(s)

CODEN: JBCHA3 ISSN: 0021-9258
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 2003:37345999 BIOTECHNO
AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p determines its in vivo prion properties and in vitro **amyloid**-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diameter** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diameters** of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning transmission electron microscopy (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.

L44 ANSWER 2 OF 5 AGRICOLA Compiled and distributed by the National Agricultural Library of the Department of Agriculture of the United States of America. It contains copyrighted materials. All rights reserved. (2004) on STN DUPLICATE 1
ACCESSION NUMBER: 2002:50889 AGRICOLA
DOCUMENT NUMBER: IND23281705
TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein.
AUTHOR(S): Baxa, U.; Speransky, V.; Steven, A.C.; Wickner, R.B.
AVAILABILITY: DNAL (500 N21P)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, Apr 16, 2002. Vol. 99, No. 8. p. 5253-5260
Publisher: Washington, D.C. : National Academy of Sciences,
CODEN: PNASA6; ISSN: 0027-8424
NOTE: Includes references
PUB. COUNTRY: District of Columbia; United States
DOCUMENT TYPE: Article; Conference
FILE SEGMENT: U.S. Imprints not USDA, Experiment or Extension
LANGUAGE: English
AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diameters** increased with the mass of the appended enzyme. The

helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all beta-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

L44 ANSWER 3 OF 5 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 2
ACCESSION NUMBER: 1999:39603 LIFESCI
TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
AUTHOR: Taylor, K.L.; Cheng, Naiqian; Williams, R.W.; Steven, A.C.; Wickner, R.B.*
CORPORATE SOURCE: Lab. Biochem. and Genet., Natl. Inst. Health, Bethesda, MD 20892-0830, USA; E-mail: wickner@helix.nih.gov
SOURCE: Science (Washington) [Science (Wash.)], (19990226) vol. 283, no. 5406, pp. 1339-1343.
ISSN: 0036-8075.
DOCUMENT TYPE: Journal
FILE SEGMENT: K; V
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The [URE3] non-Mendelian genetic element of Saccharomyces cerevisiae is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p super(1-65) were shown to polymerize to form **filaments** 40 to 45 angstroms in **diameter** with more than 60 percent beta sheet. Ure2p specifically induced full-**length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in extracts of [URE3] strains, these 180- to 220-angstrom-**diameter filaments** were protease resistant. The Ure2p super(1-65)-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular **filaments**. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].

L44 ANSWER 4 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1991:21180842 BIOTECHNO
TITLE: Morphology and antibody recognition of synthetic β- **amyloid** peptides
AUTHOR: Fraser P.E.; Duffy L.K.; O'Malley M.B.; Nguyen J.; Inouye H.; Kirschner D.A.
CORPORATE SOURCE: Neurology Research, Children's Hospital, Enders 2, 320 Longwood Ave.,Boston, MA 02115, United States.
SOURCE: Journal of Neuroscience Research, (1991), 28/4 (474-485)
CODEN: JNREDK ISSN: 0360-4012
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
AN 1991:21180842 BIOTECHNO
AB To elucidate the relationship between **amyloid** fibril formation in Alzheimer disease (AD) and the primary structure of the β-**amyloid** protein (β-AP), we investigated the ability of peptides sharing sequences with β-AP to form fibrils in vitro and to recognize anti-β- **amyloid** antisera. The peptides, which

were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full **length** of β-AP. Electron microscopy of negative-stained or thin-sectioned preparations revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD **amyloid**. Peptide 6-25 fibrils had **diameters** of 50-80 Å and occasionally showed a central groove suggestive of constituent **filaments**. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with **diameters** of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1,100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in **diameter**. When the peptide **assemblies** were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross-β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native **amyloid** or to synthetic peptide β-(1-28) was highly reactive in an inhibition-ELISA assay to β-(6-25) and β-(1-38), but not to β-(22-35), and immunostained β-(1-40) on Western blots. These studies show that the β-(6-25), β-(1-38) and β-(1-40) peptides can assemble into cross-β fibrils that retain epitopes characteristic of AD **amyloid**.

L44 ANSWER 5 OF 5 BIOTECHNO COPYRIGHT 2004 Elsevier Science B.V. on STN
DUPLICATE
ACCESSION NUMBER: 1985:15068440 BIOTECHNO
TITLE: Identification of prion **amyloid** **filaments** in scrapie-infected brain
AUTHOR: DeArmond S.J.; McKinley M.P.; Barry R.A.; et al.
CORPORATE SOURCE: Department of Pathology, University of California, San Francisco, CA 94143, United States.
SOURCE: Cell, (1985), 41/1 (221-235)
CODEN: CELLB5
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
AN 1985:15068440 BIOTECHNO
AB Extracellular collections of abnormal **filaments** composed of prion proteins have been identified in the brains of scrapie-infected hamsters using immuno-electron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same **diameter** and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **filaments** and rods are composed of PrP 27-30 molecules, and determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.

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L48 2 FILE EMBASE
L49 50 FILE USPATFULL

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L50 59 (CAG REPEAT) AND (HUNTINGTON OR DRPLA OR ATAXIN) AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH

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L51 5 DUP REM L45-L48 (4 DUPLICATES REMOVED)

=> d l51 ibib abs total

L51 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:716876 CAPLUS
DOCUMENT NUMBER: 139:287912
TITLE: **Ataxin**-3 interactions with Rad23 and valosin-containing protein and its associations with ubiquitin chains and the proteasome are consistent with a role in ubiquitin-mediated proteolysis
AUTHOR(S): Doss-Pepe, Ellen W.; Stenroos, Edward S.; Johnson, William G.; Madura, Kiran
CORPORATE SOURCE: Department of Biochemistry, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, Piscataway, NJ, 08854, USA
SOURCE: Molecular and Cellular Biology (2003), 23(18), 6469-6483
CODEN: MCEBD4; ISSN: 0270-7306
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Machado-Joseph disease is caused by an expansion of a trinucleotide **CAG repeat** in the gene encoding the protein **ataxin**-3. We investigated whether **ataxin**-3 is a

proteasome-associated factor that recognizes ubiquitinated substrates on the basis on the following information: (i) it is present with proteasome subunits and ubiquitin in cellular inclusions; (ii) it interacts with human Rad23, a protein that may translocate proteolytic substrates to the proteasome; and (iii) it shares regions of sequence similarity with the proteasome subunit S5a, which can recognize multiubiquitinated proteins. We report that **ataxin**-3 interacts with ubiquitinated proteins, can bind the proteasome, and when the gene harbors an expanded repeat **length**, can interfere with the degradation of a well-characterized test substrate. Addnl., **ataxin**-3 assocs. with the ubiquitin- and proteasome-binding factors Rad23 and valosin-containing protein (VCP/p97), findings that support the hypothesis that **ataxin**-3 is a proteasome-associated factor that mediates the degradation of ubiquitinated proteins.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 2 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:278678 BIOSIS
DOCUMENT NUMBER: PREV200200278678
TITLE: Remedy for **CAG repeat** expansion diseases.
AUTHOR(S): Tsuji, Shoji [Inventor, Reprint author]
CORPORATE SOURCE: Niigata, Japan
ASSIGNEE: Niigata University, Japan
PATENT INFORMATION: US 6355690 March 12, 2002
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Mar. 12, 2002) Vol. 1256, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 8 May 2002
Last Updated on STN: 8 May 2002

AB To elucidate the molecular mechanisms of "gain of toxic function" of expanded polyglutamine stretches in **CAG repeat** expansion diseases, the inventors established an expression system of full-**length** and truncated cDNAs for dentatorubral-pallidoluysian atrophy (**DRPLA**) and found that truncated **DRPLA** proteins containing the expanded polyglutamine stretch, but not the full-**length** protein, form peri- and intra-nuclear aggregates consisting of **filaments** and concomitant apoptosis. The apoptotic cell death was partially suppressed by transglutaminase inhibitors, cystamine and monodansyl cadaverine, raising the possibility of involvement of transglutaminase reaction. The results may provide a potential basis for the development of therapeutic measures for **CAG repeat** expansion diseases.

L51 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2002:362711 CAPLUS
DOCUMENT NUMBER: 137:92006
TITLE: Amyloid-like Features of Polyglutamine Aggregates and Their **Assembly** Kinetics
AUTHOR(S): Chen, Songming; Berthelier, Valerie; Hamilton, J. Bradley; O'Nuallain, Brian; Wetzel, Ronald
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, Knoxville, TN, 37920, USA
SOURCE: Biochemistry (2002), 41(23), 7391-7399 CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The repeat **length**-dependent tendency of the polyglutamine sequences of certain proteins to form aggregates may underlie the

cytotoxicity of these sequences in expanded **CAG repeat** diseases such as **Huntington**'s disease. The authors report here a number of features of various polyglutamine (polyGln) aggregates and their **assembly** pathways that bear a resemblance to generally recognized defining features of amyloid fibrils. PolyGln aggregation kinetics displays concentration and **length** dependence and a lag phase that can be abbreviated by seeding. PolyGln aggregates exhibit classical β-sheet-rich CD spectra consistent with an amyloid-like substructure. The fundamental structural unit of all the in vitro aggregates described here is a **filament** about 3 nm in width, resembling the protofibrillar intermediates in amyloid fibril **assembly**. The authors observed these filamentous structures either as isolated threads, as components of ribbonlike sheets, or, rarely, in amyloid-like twisted fibrils. All of the polyGln aggregates described here bind thioflavin T and shift its fluorescence spectrum. Although all polyGln aggregates tested bind the dye Congo red, only aggregates of a relatively long polyGln peptide exhibit Congo red birefringence, and this birefringence is only observed in a small portion of these aggregates. Remarkably, a monoclonal antibody with high selectivity for a generic amyloid fibril conformational epitope is capable of binding polyGln aggregates. Thus, polyGln aggregates exhibit most of the characteristic features of amyloid, but the twisted fibril structure with Congo red birefringence is not the predominant form in the polyGln repeat **length** range studied here. The authors also find that polyGln peptides exhibit an unusual freezing-dependent aggregation that appears to be caused by the freeze concentration of peptide and/or buffer components. This is of both fundamental and practical significance. PolyGln aggregation is revealed to be a highly specific process consistent with a significant degree of order in the mol. structure of the product. This ordered structure, or the **assembly** process leading to it, may be responsible for the cell-specific neuronal degeneration observed in **Huntington**'s and other expanded **CAG repeat** diseases.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L51 ANSWER 4 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2001:433998 BIOSIS
DOCUMENT NUMBER: PREV200100433998
TITLE: A microtiter plate assay for polyglutamine aggregate extension.
AUTHOR(S): Berthelier, Valerie; Hamilton, J. Bradley; Chen, Songming; Wetzel, Ronald [Reprint author]
CORPORATE SOURCE: Graduate School of Medicine, University of Tennessee Medical Center, 1924 Alcoa Highway, R221, Knoxville, TN, 37920, USA
SOURCE: Analytical Biochemistry, (August 15, 2001) Vol. 295, No. 2, pp. 227-236. print.
CODEN: ANBCA2. ISSN: 0003-2697.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Sep 2001
Last Updated on STN: 22 Feb 2002

AB Polyglutamine (polyGln) aggregates are neuropathological markers of expanded **CAG repeat** disorders, and may also play a critical role in the development of these diseases. We have established a highly sensitive, fast, reproducible, and specific assay capable of monitoring aggregate-dependent deposition of polyglutamine peptides. This assay allows detailed studies on various aspects of aggregation kinetics, and also makes possible the detection and quantitation of low levels of "extension-competent" aggregates. In the simplest form of this assay, polyGln aggregates are made from chemically synthesized peptides and immobilized onto microplate wells. These wells are incubated for different times with low concentrations of a soluble biotinylated polyGln peptide. Europium-streptavidin complexation of the immobilized biotin,

followed by time-resolved fluorescence detection of the deposited europium, allows us to calculate the rate (fmol/h) of incorporation of polyGln peptides into polyGln aggregates. This assay will make possible basic studies on the **assembly** mechanism of polyGln aggregates and on critical features of the reaction, such as polyGln **length** dependence. The assay also will be a valuable tool for screening and characterizing anti-aggregation inhibitors. It will also be useful for detection and quantitation of aggregation-competent polyGln aggregates in biological materials, which may prove to be of critical importance in understanding the disease mechanism.

L51 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
DUPLICATE 2
ACCESSION NUMBER: 1999:180905 BIOSIS
DOCUMENT NUMBER: PREV199900180905
TITLE: Expanded polyglutamine domain proteins bind neurofilament and alter the neurofilament network.
AUTHOR(S): Nagai, Yoshitaka; Onodera, Osamu; Chun, Jerold; Strittmatter, Warren J.; Burke, James R. [Reprint author]
CORPORATE SOURCE: Department of Medicine (Neurology), Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Experimental Neurology, (Feb., 1999) Vol. 155, No. 2, pp. 195-203. print.
CODEN: EXNEAC. ISSN: 0014-4886.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 May 1999
Last Updated on STN: 5 May 1999

AB Eight inherited neurodegenerative diseases are caused by genes with expanded **CAG repeats** coding for polyglutamine domains in the disease-producing proteins. The mechanism by which this expanded polyglutamine domain causes neurodegenerative disease is unknown, but nuclear and cytoplasmic polyglutamine protein aggregation is a common feature. In transfected COS7 cells, expanded polyglutamine proteins aggregate and disrupt the vimentin intermediate **filament** network. Since neurons have an intermediate **filament** network composed of neurofilament (NF) and NF abnormalities occur in neurodegenerative diseases, we examined whether pathologic-**length** polyglutamine domain proteins also interact with NF. We expressed varying **lengths** polyglutamine-green fluorescent protein fusion proteins in a neuroblast cell line, TR1. Pathologic-**length** polyglutamine-GFP fusion proteins formed large cytoplasmic aggregates surrounded by neurofilament. Immunoisolation of pathologic-**length** polyglutamine proteins coisolated 68-kDa NF protein demonstrating molecular interaction. These observations suggest that polyglutamine interaction with NF is important in the pathogenesis of the polyglutamine repeat diseases.

=> amyloid and (filament or aggregrate or assembly) and length and diameter
L52 11 FILE CAPLUS
L53 8 FILE BIOSIS
L54 9 FILE MEDLINE
L55 10 FILE EMBASE
L56 793 FILE USPATFULL

TOTAL FOR ALL FILES
L57 831 AMYLOID AND (FILAMENT OR AGGREGRATE OR ASSEMBLY) AND LENGTH AND DIAMETER

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ENTER L# LIST OR (END):l52-l55
PROCESSING COMPLETED FOR L52
PROCESSING COMPLETED FOR L53

PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L55
L58 16 DUP REM L52-L55 (22 DUPLICATES REMOVED)

=> d l58 ibib abs total

L58 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:495393 CAPLUS
DOCUMENT NUMBER: 141:201912
TITLE: The formation of straight and twisted **filaments** from short tau peptides
AUTHOR(S): Goux, Warren J.; Kopplin, Lauren; Nguyen, Anh D.; Leak, Kathryn; Rutkofsky, Marni; Shanmuganandam, Vasanthi D.; Sharma, Deepak; Inouye, Hideyo; Kirschner, Daniel A.
CORPORATE SOURCE: Department of Chemistry, the University of Texas at Dallas, Richardson, TX, 75083-0688, USA
SOURCE: Journal of Biological Chemistry (2004), 279(26), 26868-26875
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We studied fibril formation in a family of peptides based on PHF6 (VQIVYK), a short peptide segment found in the microtubule binding region of tau protein. N-Acetylated peptides AcVYK-amide (AcVYK), AcIVYK-amide (AcPHF4), AcQIVYK-amide (AcPHF5), and AcV-QIVYK-amide (AcPHF6) rapidly formed straight **filaments** in the presence of 0.15 M NaCl, each composed of two laterally aligned protofilaments .apprx.5 nm in width. X-ray fiber diffraction showed the omnipresent sharp 4.7-Å reflection indicating that the scattering objects are likely elongated along the hydrogen-bonding direction in a cross-β conformation, and Fourier transform IR suggested the peptide chains were in a parallel (AcVYK, AcPHF6) or antiparallel (AcPHF4, AcPHF5) β-sheet configuration. The dipeptide N-acetyl-YK-amide (AcYK) formed globular structures .apprx.200 nm to 1 μm in **diam**. The polymerization rate, as measured by thioflavin S binding, increased with the **length** of the peptide going from AcYK → AcPHF6, and peptides that aggregated most rapidly displayed CD spectra consistent with β-sheet structure. There was a 3-fold decrease in rate when Val was substituted for Ile or Gln, nearly a 10-fold decrease when Ala was substituted for Tyr, and an increase in polymerization rate when Glu was substituted for Lys. Twisted **filaments**, composed of four laterally aligned protofilaments (9-19 nm width, .apprx.90 nm half-periodicity), were formed by mixing AcPHF6 with AcVYK. Taken together these results suggest that the core of PHF6 is localized at VYK, and the interaction between small amphiphilic segments of tau may initiate nucleation and lead to **filaments** displaying paired helical **filament** morphol.
REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:160995 BIOSIS
DOCUMENT NUMBER: PREV200400164922
TITLE: Formation of **amyloid** from superoxide dismutase.
AUTHOR(S): Oztug, Zeynep [Reprint Author]; Padua, Shelby [Reprint Author]; Downes, Sean [Reprint Author]; Cohlberg, Jeffrey A. [Reprint Author]; Rodriguez, Jorge; Doucette, Peter; Valentine, Joan S.
CORPORATE SOURCE: Dept of Chemistry and Biochemistry, California State University, Long Beach, Long Beach, CA, USA
SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

504a. print.
Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004. Biophysical Society.
ISSN: 0006-3495 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Mar 2004
Last Updated on STN: 24 Mar 2004

AB Mutations in copper-zinc superoxide dismutase (SOD) are the cause of 20 percent of the cases of familial amyotrophic lateral sclerosis (FALS). Insoluble deposits containing SOD are found in motor neurons of FALS patients, some of which are reactive with the **amyloid**-specific dye thioflavin S. It has been proposed that the mutations cause the disease by increasing the tendency of SOD to aggregate. Furthermore, certain SOD crystal structures show linear arrays of SOD dimers similar to **amyloid filaments**. Therefore, conditions were sought under which SOD forms **amyloid**. Protein solutions were agitated at 37C in the presence of thioflavin T, and **amyloid** formation was detected by monitoring fluorescence with a microplate reader. Wild-type SOD formed **amyloid** at pH 3 and 0.5-2 M guanidine hydrochloride, with an optimum of about 1 M guanidine. The kinetics showed a lag phase of variable **length**, typically about 24 hr, followed by a rise in fluorescence over a period of a few hours. Incubation of the product with Congo Red produced a shift in the absorbance peak from 510 nm to 542 nm. Transmission electron microscopy revealed straight **filaments** with **diameters** of about 10 nm, often appearing as bundles up to 50 nm in **diameter**. Apo-SOD did not form **amyloid** under these conditions. Various FALS-related mutant SODs also formed **amyloid filaments** at acidic pH and low concentrations of guanidine. For some of the mutants less acidic conditions were required to promote **amyloid** formation. Under some conditions, mutant SODs formed **amyloid** only when seeded by preexisting **amyloid**, while seeding appeared to have no effect with other samples. 30% acetonitrile can substitute for guanidine hydrochloride in promoting **amyloid** formation. The results may be relevant to the aggregation of SOD which occurs in motor neurons in FALS.

L58 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:660806 CAPLUS
TITLE: Nanostructure of β-sheet fibrils constructed by unfolded β-hairpin peptide self- **assembly**
AUTHOR(S): Lamm, Matthew S.; Rajagopal, Karthikan; Schneider, Joel P.; Pochan, Darrin J.
CORPORATE SOURCE: Department of Materials Science and Engineering, University of Delaware, Newark, DE, 19716, USA
SOURCE: Abstracts of Papers, 228th ACS National Meeting, Philadelphia, PA, United States, August 22-26, 2004 (2004), POLY-345. American Chemical Society: Washington, D. C.
CODEN: 69FTZ8
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English

AB A 20-residue peptide consisting of alternating valine and lysine residues flanking a tripeptide turn sequence has been shown to self-assemble via differing pathways into dramatically different materials, depending on the primary structure of the turn sequence. Under appropriate solution conditions, peptides with type II' turn sequences intramolecularly fold leading to β-sheet rich, reversible hydrogelation. Alternatively, almost identical peptides, differing only in turn sequence that strongly disfavors intramol. folding, adopt an extended β-sheet conformation and irreversibly assemble into β- **amyloid**-like, prion-like

fibrillar structures. The resulting fibrillar structures are analyzed using transmission electron microscopy, atomic force microscopy and x-ray diffraction; an untwisted, un-branched morphol. is observed characterized by lateral **assembly** of .apprx.2.5nm **diam.** **filaments** and up to microns in **length**. Lateral association of **filaments** produced fibril widths of 100nm or more. Each fibril has an exact height of .apprx.6.7nm suggesting that each peptide is in an extended conformation with the peptide backbone orthogonal to both the fibril axis and the direction of lamination.

L58 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:850847 CAPLUS
DOCUMENT NUMBER: 140:2085
TITLE: Architecture of Ure2p Prion **Filaments**: the N-terminal domains form a central core fiber
AUTHOR(S): Baxa, Ulrich; Taylor, Kimberly L.; Wall, Joseph S.; Simon, Martha N.; Cheng, Naiqian; Wickner, Reed B.; Steven, Alasdair C.
CORPORATE SOURCE: Lab. Struct. Biol., Natl. Inst. Arthritis, Musculoskeletal, and Skin Dis., Natl. Inst. Health, Bethesea, MD, 20892, USA
SOURCE: Journal of Biological Chemistry (2003), 278(44), 43717-43727
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The [URE3] prion is an inactive, self-propagating, filamentous form of the Ure2 protein, a regulator of nitrogen catabolism in yeast. The N-terminal "prion" domain of Ure2p dets. its in vivo prion properties and in vitro **amyloid**-forming ability. Here we determined the overall structures of Ure2p **filaments** and related polymers of the prion domain fused to other globular proteins. Protease digestion of 25-nm **diam.** Ure2p **filaments** trimmed them to 4-nm **filaments**, which mass spectrometry showed to be composed of prion domain fragments, primarily residues .apprx.1-70. Fusion protein **filaments** with **diams**. of 14-25 nm were also reduced to 4-nm **filaments** by proteolysis. The prion domain transforms from the most to the least protease-sensitive part upon **filament** formation in each case, implying that it undergoes a conformational change. Intact **filaments** imaged by cryo-electron microscopy or after vanadate staining by scanning TEM (STEM) revealed a central 4-nm core with attached globular appendages. STEM mass per unit **length** measurements of unstained **filaments** yielded 1 monomer per 0.45 nm in each case. These observations strongly support a unifying model whereby subunits in Ure2p **filaments**, as well as in fusion protein **filaments**, are connected by interactions between their prion domains, which form a 4-nm **amyloid filament** backbone, surrounded by the corresponding C-terminal moieties.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:72748 CAPLUS
DOCUMENT NUMBER: 136:146104
TITLE: Human stress genes identified using DNA microarrays
INVENTOR(S): Chenchik, Alex; Lukashev, Matvey E.
PATENT ASSIGNEE(S): Clontech, USA
SOURCE: U.S. Pat. Appl. Publ., 57 pp., Cont.-in-part of U.S. Ser. No. 441,920.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002009730	A1	20020124	US 2001-782909	20010213
PRIORITY APPLN. INFO.:			US 1998-222256 B2	19981228
			US 1999-440305 B2	19991117
			US 1999-441920 A2	19991117

AB Human stress arrays and methods for their use are provided. The subject arrays include a plurality of polynucleotide spots, each of which is made up of a polynucleotide probe composition of unique polynucleotides corresponding to a human stress gene. The average **length** of the polynucleotide probes is between 50 to 1000 nucleotides. The d. of the spots on the array did not exceed 400/cm2 and the spots had a **diam**. ranging between 10 to 5000 μm. Furthermore, the number of polynucleotide probe spots on the array ranged between 50 to 2000 nucleotides. The subject arrays find use in hybridization assays, particularly in assays for the identification of differential gene expression of human stress genes. 236 Different human stress genes were identified using this approach.

L58 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:316601 CAPLUS
DOCUMENT NUMBER: 137:45099
TITLE: Mechanism of inactivation on prion conversion of the Saccharomyces cerevisiae Ure2 protein
AUTHOR(S): Baxa, Ulrich; Speransky, Vladislav; Steven, Alasdair C.; Wickner, Reed B.
CORPORATE SOURCE: Laboratories of Structural Biology, National Institute of Arthritis, Musculoskeletal Diseases, and Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(8), 5253-5260
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The [URE3] infectious protein (prion) of Saccharomyces cerevisiae is a self-propagating **amyloid** form of Ure2p. The C-terminal domain of Ure2p controls nitrogen catabolism by complexing with the transcription factor, Gln3p, whereas the asparagine-rich N-terminal "prion" domain is responsible for **amyloid filament** formation (prion conversion). On **filament** formation, Ure2p is inactivated, reflecting either a structural change in the C-terminal domain or steric blocking of its interaction with Gln3p. We fused the prion domain with four proteins whose activities should not be sterically impeded by aggregation because their substrates are very small: barnase, carbonic anhydrase, glutathione S-transferase, and green fluorescent protein. All formed **amyloid filaments** in vitro, whose **diams**. increased with the mass of the appended enzyme. The helical repeat **lengths** were consistent within a single **filament** but varied with the construct and between **filaments** from a single construct. CD data suggest that, in the soluble fusion proteins, the prion domain has no regular secondary structure, whereas earlier data showed that in **filaments**, it is virtually all β-sheet. In **filaments**, the activity of the appended proteins was at most mildly reduced, when substrate diffusion effects were taken into account, indicating that they retained their native structures. These observations suggest that the **amyloid** content of these **filaments** is confined to their prion domain-containing backbones and imply that Ure2p is inactivated in [URE3] cells by a steric blocking mechanism.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:703452 CAPLUS
DOCUMENT NUMBER: 138:2785
TITLE: Examining the structure of the mature **amyloid** fibril
AUTHOR(S): Makin, O. S.; Serpell, L. C.
CORPORATE SOURCE: Structural Medicine Unit, Cambridge Institute for Medical Research, Cambridge, CB2 2XY, UK
SOURCE: Biochemical Society Transactions (2002), 30(4), 521-525
CODEN: BCSTB5; ISSN: 0300-5127
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The pathogenesis of the group of diseases known collectively as the amyloidoses is characterized by the deposition of insol. **amyloid** fibrils. These are straight, unbranching structures about 70-120 Å (1 Å = 0.1 nm) in diam. and of indeterminate **length** formed by the self-**assembly** of a diverse group of normally soluble proteins. Knowledge of the structure of these fibrils is necessary for the understanding of their abnormal **assembly** and deposition, possibly leading to the rational design of therapeutic agents for their prevention or disaggregation. Structural elucidation is impeded by fibril insoly. and inability to crystallize, thus preventing the use of x-ray crystallog. and solution NMR. CD, Fourier-transform IR spectroscopy and light scattering have been used in the study of the mechanism of fibril formation. This review concs. on the structural information about the final, mature fibril and in particular the complementary techniques of cryo-electron microscopy, solid-state NMR and x-ray fiber diffraction.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 8 OF 16 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001241576 EMBASE
TITLE: Yeast prions act as genes composed of self-propagating protein **amyloids**.
AUTHOR: Wickner R.B.; Taylor K.L.; Edskes H.K.; Maddelein M.-L.; Moriyama H.; Tibor Roberts B.
CORPORATE SOURCE: R.B. Wickner, Laboratory of Biochemistry, Natl. Inst. Diab. Digest./Kid. Dis., National Institutes of Health, Bethesda, MD 20892, United States
SOURCE: Advances in Protein Chemistry, (2001) 57/- (313-334).
Refs: 71
ISSN: 0065-3233 CODEN: APCHA2
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We proposed genetic properties by which prions can be recognized among infectious elements. This indicated that [URE3] and [PSI], two nonchromosomal genetic elements of yeast, were prions (infectious altered forms) of Ure2p and Sup35p, respectively. Overexpression of Ure2p leads to the de novo appearance of the [URE3] prion, and the N-terminal 65-80 residues (the prion domain) are specifically responsible for this prion-inducing activity. The prion domain is sufficient to propagate [URE3] and is necessary for a Ure2p molecule to be affected by [URE3]. The remaining C-terminal residues 81-354 are responsible for nitrogen catabolite repression, the normal function of Ure2p. Ure2p is protease-resistant specifically in extracts of [URE3] strains and is

aggregated in vivo specifically in such strains. The chemically synthesized Ure2p prion domain (Ure2p(1-65)) spontaneously forms classic **amyloid filaments** (50 A diameter) in vitro, and specifically induces the native full **length** Ure2p to form a 1:1 **amyloid** cofilament (200 A). These **amyloid** cofilaments can prime amyoid **filament** formation by an excess of native Ure2p. The features of the in vitro **amyloid** propagation reaction appear to reproduce the in vivo properties of [URE3] prion propagation. This system may be useful for detecting new prions, finding **amyloid**-inducing and amyloid-curing agents, and determining the cellular components that affect the initiation and propagation of infectious amyloids. The [Het-s] prion was found in the filamentous fungus Podospora anserina by similar genetic tests to those we used for [URE3] and [PSI]. [Het-s] is necessary for a normal function of Podospora cells, heterokaryon incompatibility. This suggests that other normal cellular functions may involve a prion-like mechanism.

L58 ANSWER 9 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:80946 BIOSIS
DOCUMENT NUMBER: PREV200100080946
TITLE: A de novo designed helix-turn-helix peptide forms nontoxic **amyloid** fibrils.
AUTHOR(S): Fezoui, Y. [Reprint author]; Hartley, D. M.; Walsh, D. M.; Selkoe, D. J.; Osterhout, J. J.; Teplow, D. B.
CORPORATE SOURCE: Brigham and Women's Hospital, Boston, MA, USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No. 1-2, pp. Abstract No.-299.9. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience. New Orleans, LA, USA. November 04-09, 2000. Society for Neuroscience.
ISSN: 0190-5295.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 14 Feb 2001
Last Updated on STN: 12 Feb 2002

AB During fibrillogenesis studies of the **amyloid** beta-protein (Abeta), we sought a non-amyloidogenic "negative control" peptide. Prior work suggested that alphatalpha, a de novo designed, monomeric, 38-residue alpha-helix-turn-alpha-helix peptide would be ideal. alphatalpha was developed as a model for the study of protein folding intermediates and has a protein-like sequence and a stable tertiary structure. At pH 3.6 and pH 10.5, alphatalpha showed no aggregation after 8 weeks of incubation at 37degreeC. Surprisingly, at neutral pH, alphatalpha formed fibrils after 2 days of incubation at 37degreeC. Negative staining and electron microscopy revealed non-branching fibril **assemblies** 6-10 nm in width, which varied in length from 200 to 1200 nm. These **assemblies** were composed of two or more **filaments**, each 3-3.5 nm in **diameter**, and had the appearance of narrow ribbons. These types of structures also formed during the fibrillogenesis of Abeta and of the islet **amyloid** polypeptide (IAPP), however the rope-like, bifilar structures often seen in fibrils of Abeta and IAPP were not observed in alphatalpha fibrils. In common with the fibrillogenesis of Abeta and IAPP, alphatalpha fibril **assembly** involved an alpha-helixfwdarwbeta-sheet conformational change and the development of Congo red binding capacity. The shared morphologic, spectroscopic, and tinctorial properties of alphatalpha, Abeta, and IAPP fibrils suggested that alphatalpha fibrils might also share cytotoxic activity. However, alphatalpha fibrils were not toxic to cultured rat primary cortical neurons or to PC12 cells. These results suggest that the potential to form fibrils is not limited to those proteins associated with amyloidoses and that fibril formation alone is not predictive of cytotoxic activity.

L58 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1999:164136 CAPLUS
DOCUMENT NUMBER: 130:322093
TITLE: Prion domain initiation of **amyloid** formation in vitro from native Ure2p
AUTHOR(S): Taylor, Kimberly L.; Cheng, Naiqian; Williams, Robert W.; Steven, Alasdair C.; Wickner, Reed B.
CORPORATE SOURCE: Laboratory of Biochemistry and Genetics, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0830, USA
SOURCE: Science (Washington, D. C.) (1999), 283(5406), 1339-1343
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The [URE3] non-Mendelian genetic element of Saccharomyces cerevisiae is an infectious protein (prion) form of Ure2p, a regulator of nitrogen catabolism. Here, synthetic Ure2p1-65 were shown to polymerize to form **filaments** 40 to 45 angstroms in **diam.** with more than 60 % β sheet. Ure2p1-65 specifically induced full- **length** native Ure2p to copolymerize under conditions where native Ure2p alone did not polymerize. Like Ure2p in exts. of [URE3] strains, these 180- to 220-angstrom-**diam.** **filaments** were protease resistant. The Ure2p1-65-Ure2p cofilaments could seed polymerization of native Ure2p to form thicker, less regular filaments. All **filaments** stained with Congo Red to produce the green birefringence typical of **amyloid**. This self-propagating **amyloid** formation can explain the properties of [URE3].
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97327024 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9183822
TITLE: As you like it.
AUTHOR: Ghadially F N
CORPORATE SOURCE: Department of Laboratory Medicine, Ottawa Civic Hospital, Ontario, Canada.
SOURCE: Ultrastructural pathology, (1997 May-Jun) 21 (3) 211-26.
Ref: 38
Journal code: 8002867. ISSN: 0191-3123.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970805
Last Updated on STN: 19990129
Entered Medline: 19970724
AB I have developed something of a reputation for criticizing freely and frequently at our meetings and in my writings. You say you like this and find it useful and entertaining. As you like it, you are welcome to more of it. My comments and criticisms are presented under the following headings: (1) criticize at your peril; (2) how it all started (unjustly accused!); (3) abbreviations (a source of perennial aggravation, confusion, and waste of time); (4) mysterious bodies in mesotheliomas; (5) call a crystal a "crystal," not a "crystalloid"; (6) electron microscopy-a study of osmium artifacts; (7) length-to-**diameter** ratio of microvilli (mission impossible); (8) lamellar bodies (a popular

but debased term); (9) amyloid filaments, not fibers; (10) filaments and microtubules do not branch; (11) there is no such thing as pseudomelanosis; (12) botched histochemistry (just about every gastrointestinal tract pigment was misdiagnosed by histochemistry); (13) intranuclear Russell bodies, not "Dutcher bodies"; and (14) nuclear pores and virus-like particles (a new development in an old farce).

L58 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1991:245425 CAPLUS
DOCUMENT NUMBER: 114:245425
TITLE: Morphology and antibody recognition of synthetic β- amyloid peptides
AUTHOR(S): Fraser, P. E.; Duffy, L. K.; O'Malley, M. B.; Nguyen, J.; Inouye, H.; Kirschner, D. A.
CORPORATE SOURCE: Neurol. Res., Child. Hosp., Boston, MA, 02115, USA
SOURCE: Journal of Neuroscience Research (1991), 28(4), 474-85
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To elucidate the relationship between amyloid fibril formation in Alzheimer disease (AD) and the primary structure of the β-amyloid protein (β-AP), this study investigated the ability of peptides sharing sequences with β-AP to form fibrils in vitro and to recognize anti-β- amyloid antisera. The peptides, which were synthesized using a FMOC solid phase procedure and purified by HPLC, consisted of residues 6-25 from the putative aqueous domain, residues 22-35, which overlaps the putative aqueous and transmembrane domains, and residues 1-38 and 1-40 representing nearly the full length of β-AP. Electron microscopy of neg.-stained or thin-sectioned prepns. revealed that the peptides assembled into fibrils having different morphologies, some of which resembled in situ AD amyloid. Peptide 6-25 fibrils had diams. of 50-80 Å and occasionally showed a central groove suggestive of constituent filaments. Cross sections of the fibril showed a penta- or hexameric arrangement of globular subunits with diams. of 25-30 Å. Peptide 22-35 fibrils were helical, with a pitch of 1100 Å and a width of 120 Å at its greatest and 50-60 Å at its narrowest. The fibrils formed by peptides 1-38 and 1-40 were 70-90 Å in diam. When the peptide assemblies were singly oriented by sedimentation or doubly oriented in a magnetic field, their X-ray diffraction patterns all showed reflections typical of a cross-β pleated sheet conformation. The patterns differed mainly in their small-angle equatorial intensity, which arises from the packing of fibrils having different widths. Antiserum raised to either native amyloid or to synthetic peptide β-(1-28) was highly reactive in an inhibition-ELISA assay to β-(6-25) and β-(1-38), but not to β-(22-35), and immunostained β-(1-40) on Western blots. These studies show that the β-(6-25), β-(1-38) and β-(1-40) peptides can assemble into cross-β fibrils that retain epitopes characteristic of AD amyloid.

L58 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:405318 CAPLUS
DOCUMENT NUMBER: 111:5318
TITLE: Comparison of amyloid from Alzheimer's disease with synthetic peptide
AUTHOR(S): Duffy, Lawrence K.; Kirschner, Daniel A.; Joachim, Catharine L.; Sinclair, Alison; Inouye, Hideyo; Selkoe, Dennis J.
CORPORATE SOURCE: Cent. Neurol. dis., Brigham and Women's Hosp., Boston, MA, USA
SOURCE: Pept.: Chem. Biol., Proc. Am. Pept. Symp. 10th (1988), Meeting Date 1987, 604-7. Editor(s): Marshall, Garland R. ESCOM Sci. Pub.: Leiden, Neth.

CODEN: 56MDA6
DOCUMENT TYPE: Conference
LANGUAGE: English
AB X-ray patterns from partially dried, oriented pellets of β-peptide show characteristic cross β-spacings: a strong meriodional arc at 4.76 Å and a diffuse equatorial arc at 10.6 Å. These spacings and the other ones observed at wide angles are similar to those reported for β-keratin. The series of small angle intensity maximum along the equator indicate the fibril is tubular with a **diam.** of 71 Å and that the wall is composed of 2 or 3 cross β-pleated sheets. When the synthetic β-peptide **length** was increased to 45 amino acids to encompass some of the proposed membrane spanning region, it became very insol. and 88% formic acid had to be used initially to solubilize it. X-ray patterns from this peptide (β-45) in the presence of 25% trifluoroacetic acid showed β-pleated sheet spacings at about 11 Å and 4.7 Å spacings; similar but weaker patterns have been recorded for cerebral vascular **amyloid**. An analog peptide, β-28 (16-Ala) was synthesized and produced polymorphic structures whose **assemblies** were 5 or 6 β-sheets instead of 2 or 3. There was a differential inhibition loss of 20% of binding of antibody to β-28-coated plates with β-28 (16-Ala) suggesting that Lys-16 is exposed in the **amyloid** fibrils and that alanine at that position promotes intersheet stacking. Thus, the Alzheimer's disease **amyloid** behavior can be examined using synthetic peptides. A preliminary model of an **amyloid** peptide fibril is presented. Further studies using peptide analogs can be used to test this model.

L58 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1988:201098 CAPLUS
DOCUMENT NUMBER: 108:201098
TITLE: A close ultrastructural relationship between sulfated proteoglycans and AA **amyloid** fibrils
AUTHOR(S): Snow, Alan David; Willmer, Jonathan; Kisilevsky, Robert
CORPORATE SOURCE: Dep. Pathol., Queen's Univ., Kingston, ON, Can.
SOURCE: Laboratory Investigation (1987), 57(6), 687-98
CODEN: LAINAW; ISSN: 0023-6837
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two cationic reagents, ruthenium red (RR) and cuprolinic blue (CB), were used to assess the morphol. and structural relationship between sulfated proteoglycans and AA amyloid fibrils in amyloidotic spleen and liver, and in isolated fibril prepns. Amyloidotic tissue fixed in the presence of RR showed RR granules, measuring 15 to 25 nm in **diam**., over areas of electron-dense fibrils. In isolated fibril prepns., RR granules were specifically localized on **amyloid** fibrils. Amyloidotic tissue fixed in the presence of CB at 0.1M and 0.7M MgCl2 showed both granule and filamentous (50 to 90 nm in **length**) staining only over areas of amyloid fibrils. This same staining localization was also seen in isolated fibril prepns. The RR and CB granules and **filaments**, are believed to represent proteoglycan monomers with the glycosaminoglycan chains collapsed onto the protein core. The persistent CB staining at 0.7M MgCl2 suggested that highly sulfated proteoglycans were present. The glycosaminoglycan moiety has previously been identified as heparin/heparan sulfate. The intimate structural relationship between sulfated proteoglycans and AA **amyloid** fibrils, both in situ and in isolated fibril prepns., further suggests that these highly neg. charged mols. may have an important role in the pathogenesis of amyloidosis. Several pathogenetic scenarios are suggested.

L58 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1987:134807 CAPLUS
DOCUMENT NUMBER: 106:134807

TITLE: On the biology of prions
AUTHOR(S): Prusiner, S. B.; Gabizon, R.; McKinley, M. P.
CORPORATE SOURCE: Dep. Neurol., Univ. California, San Francisco, CA, 94143, USA
SOURCE: Acta Neuropathologica (1987), 72(4), 299-314
CODEN: ANPTAL; ISSN: 0001-6322
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 147 refs. Prions cause scrapie and Creutzfeldt-Jakob disease (CJD); these infectious pathogens are composed largely, if not entirely, of protein mols. No prion-specific polynucleotide has been identified. Purified prepns. of scrapie prions contain high titers (≥109.5 ID50/mL), one protein (PrP 27-30), and **amyloid** rods (10-20 nm in **diam**. + 100-200 nm in **length**). Considerable evidence indicates that PrP 27-30 is required for and inseparable from scrapie infectivity. PrP 27-30 is encoded by a cellular gene and is derived from a larger protein, denoted PrPSc or PrP 33-35Sc, by protease digestion. A cellular isoform, designated PrPC or PprP 33-35C, is encoded by the same gene as PrPSc, and both proteins appear to be translated from the same 2.1 kb mRNA. Monoclonal antibodies to PrP 27-30, as well as antisera to PrP synthetic peptides, specifically react with both PrPC and PrPSc, establishing their relatedness. PrPC is digested by proteinase K, while PrPSc is converted to PrP 27-30 under the same conditions. Prion proteins are synthesized with signal peptides and are integrated into membranes. Detergent extraction of microsomal membranes isolated from scrapie-infected hamster brains solubilizes PrPC but induces PrPSc to polymerize into **amyloid** rods. This procedure allows separation of the two prion protein isoforms and the demonstration that PrPSc accumulates during scrapie infection, while the level of PrPC does not change. The prion **amyloid** rods generated by detergent extraction are identical morphol., except for **length**, to extracellular collections of prion amyloid **filaments** which form plaques in scrapie- and CJD-infected brains. The prion **amyloid** plaques stain with antibodies to PrP 27-30 and PrP peptides. PrP 33-35C does not accumulate in the extracellular space. Prion rods composed of PrP 27-30 can be dissociated into phospholipid vesicles with full retention of scrapie infectivity. The murine PrP gene (Prn-p) is linked to the Prn-i gene which controls the **length** of the scrapie incubation period. Prolonged incubation times are a cardinal feature of scrapie and CJD. While the central role of PrPSc in scrapie pathogenesis is well established, the chemical as well as conformational differences between PrPC and PrPSc are unknown but probably arise from post-translational modifications.

L58 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 9
ACCESSION NUMBER: 1985:380799 BIOSIS
DOCUMENT NUMBER: PREV198580050791; BA80:50791
TITLE: IDENTIFICATION OF PRION **AMYLOID FILAMENTS** IN SCRAPIE-INFECTED BRAIN.
AUTHOR(S): DEARMOND S J [Reprint author]; MCKINLEY M P; BARRY R A; BRAUNFELD M B; MCCOLLOCH J R; PRUSINER S B
CORPORATE SOURCE: DEP OF PATHOLOGY, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIF 94143, USA
SOURCE: Cell, (1985) Vol. 41, No. 1, pp. 221-236.
CODEN: CELLB5. ISSN: 0092-8674.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB Extracellular collections of abnormal **filaments** composed of prion proteins were identified in the brains of scrapie-infected hamsters using immunoelectron microscopy. Some of the **filaments** were 1500 nm in **length**; generally, they exhibited a uniform **diameter** of 16 nm. Rarely, the **filaments** had a twisted

appearance, raising the possibility that they are flattened cylinders or are composed of helically wound protofilaments. The prion **filaments** possess the same diameter and limited twisting as the shorter rod-shaped particles observed in purified preparations of prions. Both the **fil**aments and rods are composed of PrP 27-30 molecules, as determined by immunoelectron microscopy using affinity-purified antibodies. The ultrastructural features of the prion **filaments** are similar to those reported for **amyloid** in many tissues including brain. These results provide the first evidence that prion proteins assemble into **filaments** within the brain and that these **filaments** accumulate in extracellular spaces to form **amyloid** plaques.